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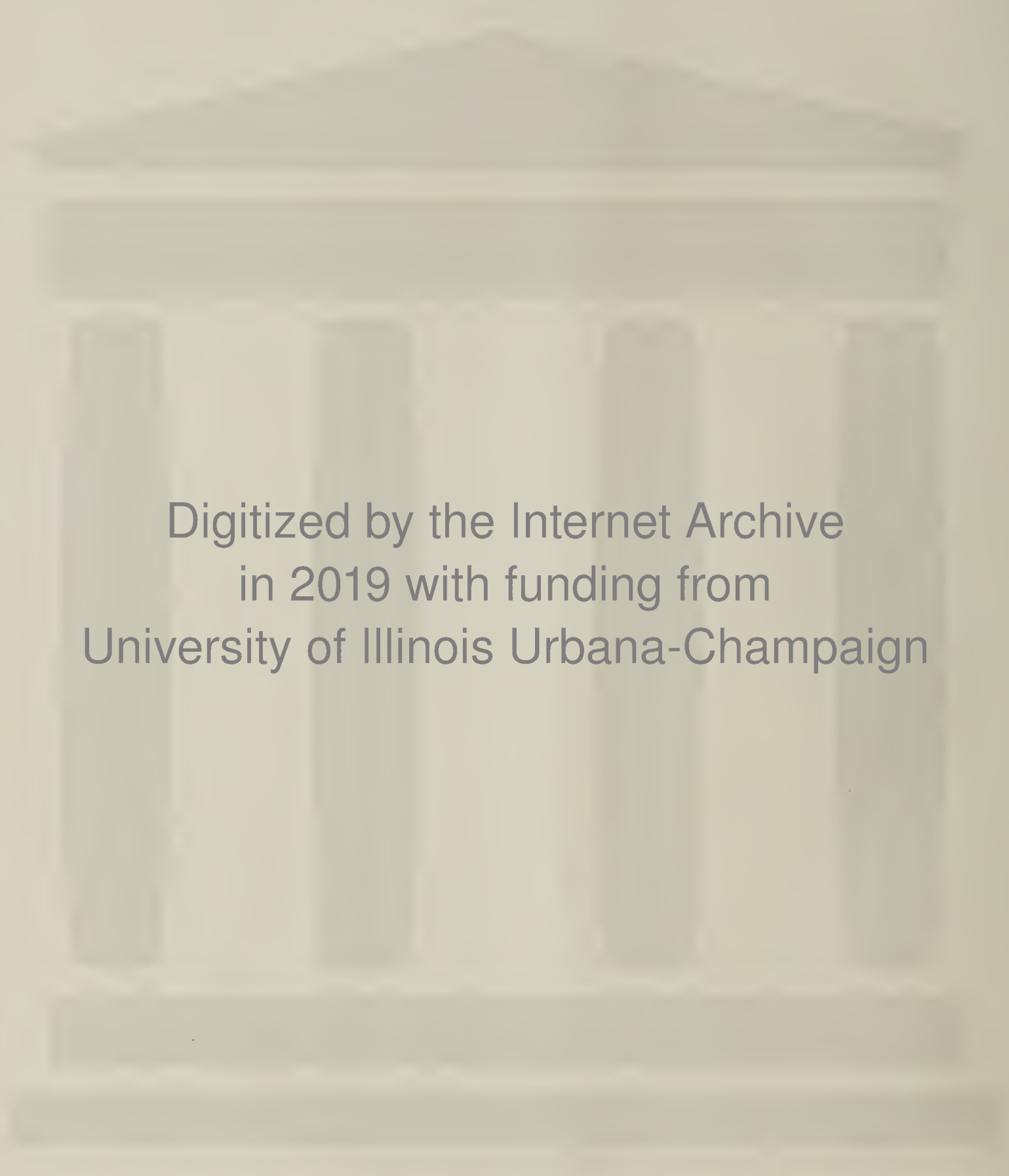


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BULLETIN

VOLUME XII

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THE REMOVAL OF PELVIC INFLAMMATORY MASSES BY THE ABDOMEN AFTER BISECTION OF THE UTERUS.¹

BY HOWARD A. KELLY, M. D.

I pointed out but recently (JOHNS HOPKINS HOSPITAL BULLETIN, 1900, XI, p. 56, and *Amer. Jour. Obst.*, 1900; XLII, August) the great advantages which accrue from the bisection of the myomatous uterus in an abdominal enucleation in certain complicated cases. I now desire to call your attention to the great value of a somewhat similar procedure in certain cases of pelvic inflammatory diseases.

In most instances of pelvic infections, the ovaries are innocently, only accidentally, involved in the inflammatory process, and as a rule one or both of them can be saved even though it is found necessary to sacrifice both uterine tubes. If one ovary is saved, the uterus must also be saved if pos-

sible, as by doing this we conserve the function of menstruation as well as that of internal secretion of the ovary.

Where the ovaries are seriously involved in the disease, where they are converted into abscess sacs or into large hematomata, or where they are so densely and intimately matted in with the inflamed tubes that it is useless to attempt to save them, the removal of all the diseased organs together with the uterus is demanded whenever it is possible in this way: by freeing the tube and the ovary on the least adherent side first, and then after tying off the broad ligament and pushing down the bladder, and securing the uterine artery, the most difficult side is easily reached and enucleated, by cutting across the cervix and exposing the opposite uterine vessels and ligating them. The uterus is then pulled up until the round ligament is caught and divided.

¹ An address delivered before The Southern Surg. & Gyn. Assoc., Atlanta, Ga., November 13, 1900.

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At this point the operation may follow one of two courses according to the difficulties encountered: in the first place, if, after dividing the uterus and pulling it up, the remaining tube and ovary can be readily enucleated by peeling them out from below upwards by working with the fingers in the lower and anterior part of the pelvis, then the enucleation may be concluded by removing all the structures in one mass. In the second place, if the tube and ovary on the far side are densely adherent and offer any serious difficulties in the enucleation, then I would clamp off the uterus at its cornu and remove it with one tube and ovary, and so leave the more difficult side to be dissected out after emptying the pelvis, securing all the advantages of increased space and light (v. Figs. 1 and 2). I have previously described this method as that of enucleation by a continuous transverse incision from left to right or from right to left.

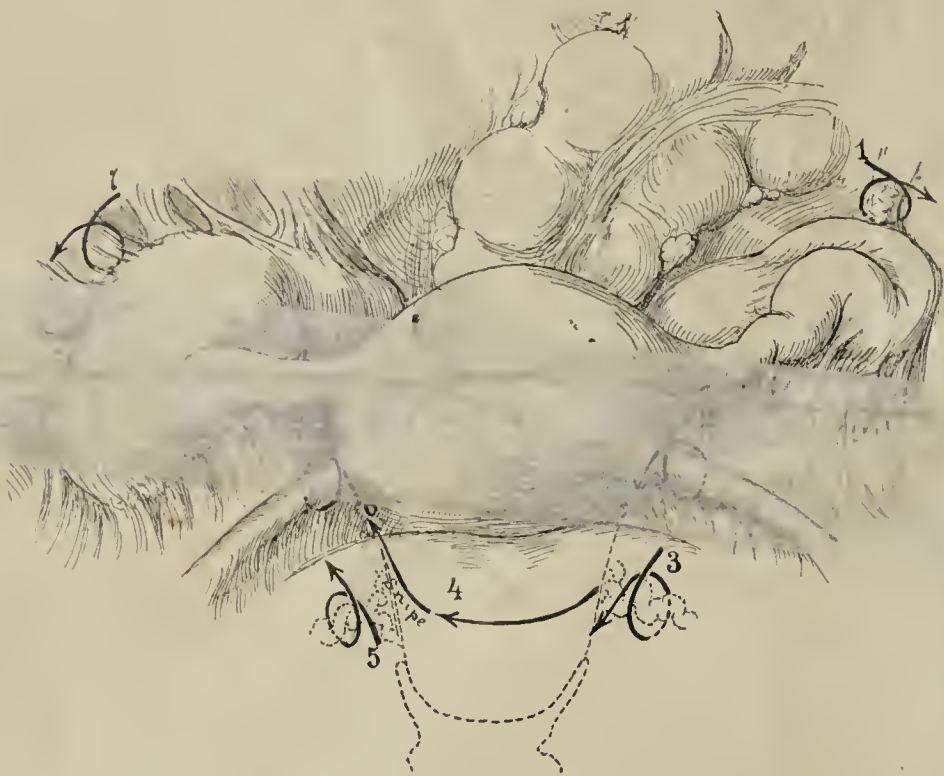


Fig. 1 shows the method of removing the uterus, in a case of pelvic inflammatory disease, by a continuous transverse incision beginning on the left side.

1 controls the left ovarian vessels.

2 controls the left round ligament; the next step is to free the vesical peritoneum from the uterus and to push the bladder down; this exposes the left uterine vessels which are now controlled by 3.

4 represents the division of the cervix exposing the right uterine vessels controlled by 5.

The division of the cervix is not directly across, a sliver or a snipe (4 to 6), is left in order to clamp the uterine vessels at a higher point.

6 is the ligature on the right round ligament and 7 that on the right ovarian vessels.

It is now my desire to describe a method of enucleation through an abdominal incision which is applicable to a class of cases still more difficult than those just referred to. Let us suppose, for example, a case in which there are *pelvic abscesses on both sides densely adherent to all the surrounding structures*, including the uterus; we will also suppose that the uterus itself is almost or quite buried in a mass of adhesions. In such a case the plan I have just described is scarcely applicable, inasmuch as there is no easier side which to begin to start the enucleation. On both sides present extreme difficulties.

The method of a continuous transverse incision does actually give us, it is true, a great advantage over the older method of tying down on both sides, for the simple reason that the enucleation of the farther side, wherever we begin, is always easier, even though the difficulties of the first side are just the same by either method.

If, now, I could devise any method by which the enucleation of *both tubes and ovaries* in such a case could be effected in a direction from below upwards, it is manifest that a great advantage would be gained.

The vaginal hysterectomists have thus far had a decided advantage over those of us who prefer to operate above the symphysis, in the greater facility with which the adherent structures can be detached when they are attacked in the direction from the pelvic floor upwards. In the method I am now about to describe, this decided advantage is secured

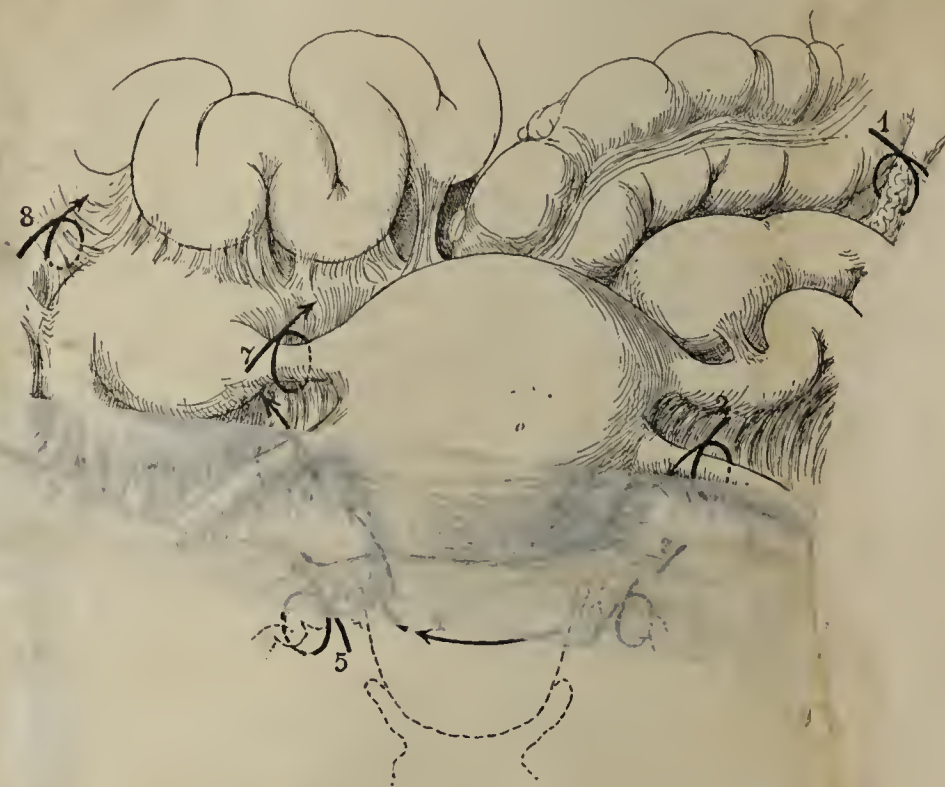


Fig. 2 shows an important modification of the method of enucleation described and shown in Fig. 1. When one side is densely adherent, first then to begin the enucleation with the opposite side in the manner described, and then after tying the round ligament at 6.

The next step then is to clamp the cornu uteri and remove the uterus with the tube and ovary of the side on which the enucleation started.

The final step in the enucleation now is to remove the dense, adherent side with forceps and scissors with all the advantages of abundant room and light afforded by the removal of the uterus.

for, and combined with the other great advantages of the abdominal route, that of increased room, and increased facilities of handling, abundant illumination, as well as the detection of various complicating conditions.

The steps are these: If the uterus is buried out of view, the bladder is first separated from the rectum and the fundus uteri found; then, if there are any large abscesses, adherent to the uterus, they are evacuated by aspiration or by incision. The rest of the abdominal cavity is then well washed out with antiseptic solution.

The next step is to clamp the cornu uteri are each seized by a pair of forceps and lifted up, the uterus is now incised in the median line in an antero-posterior direction,

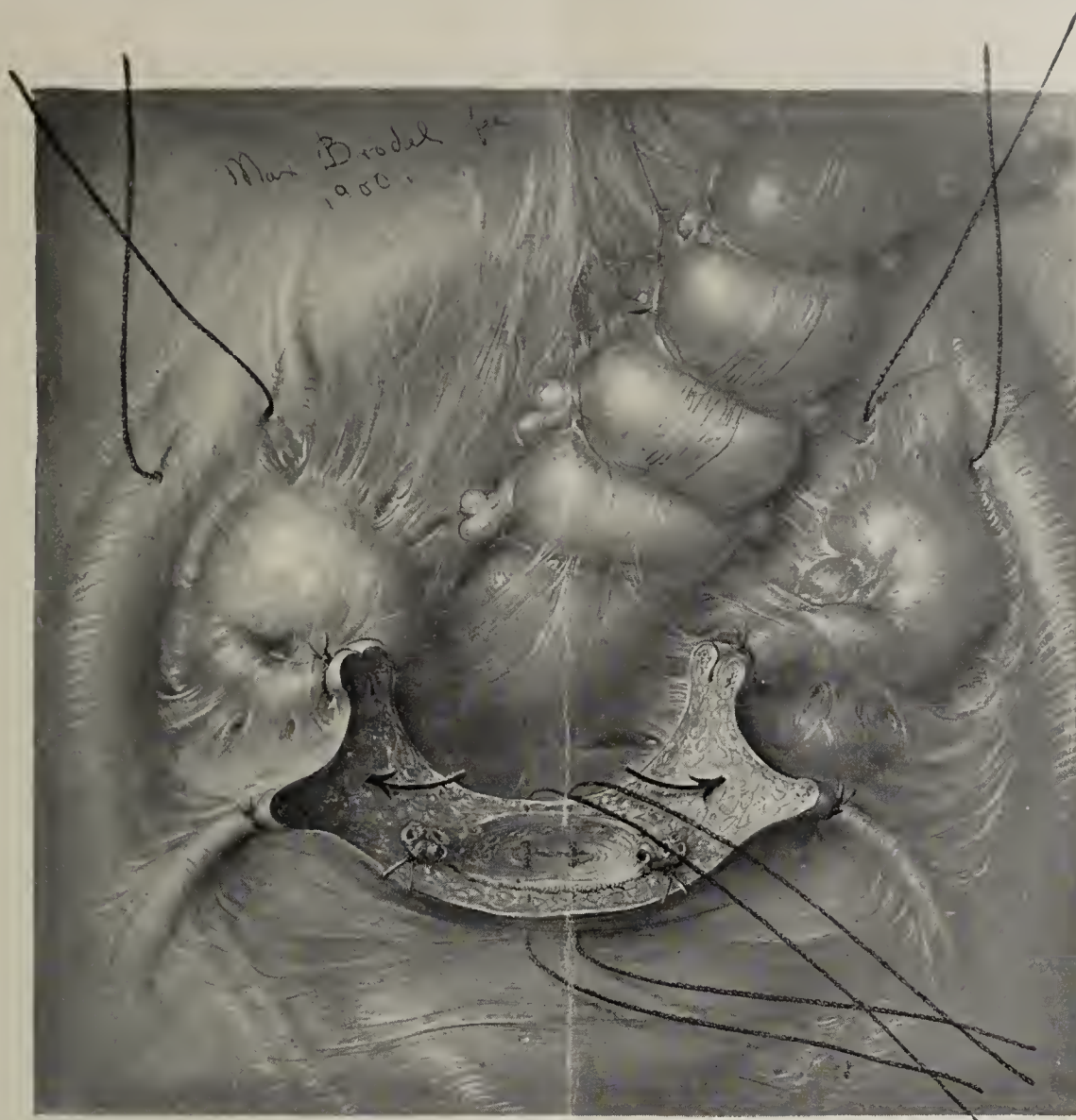


FIG. 3 shows the advantages of a bisection of the uterus enabling the surgeon to remove the uterus before removing either tube and ovary, thus affording all the conveniences of more room, abundant illumination and new avenues of approach indicated by the arrows.

Ligatures may be placed on the ovarian vessels as shown before enucleating the uterine tubes and the ovaries, when the vessels are accessible.

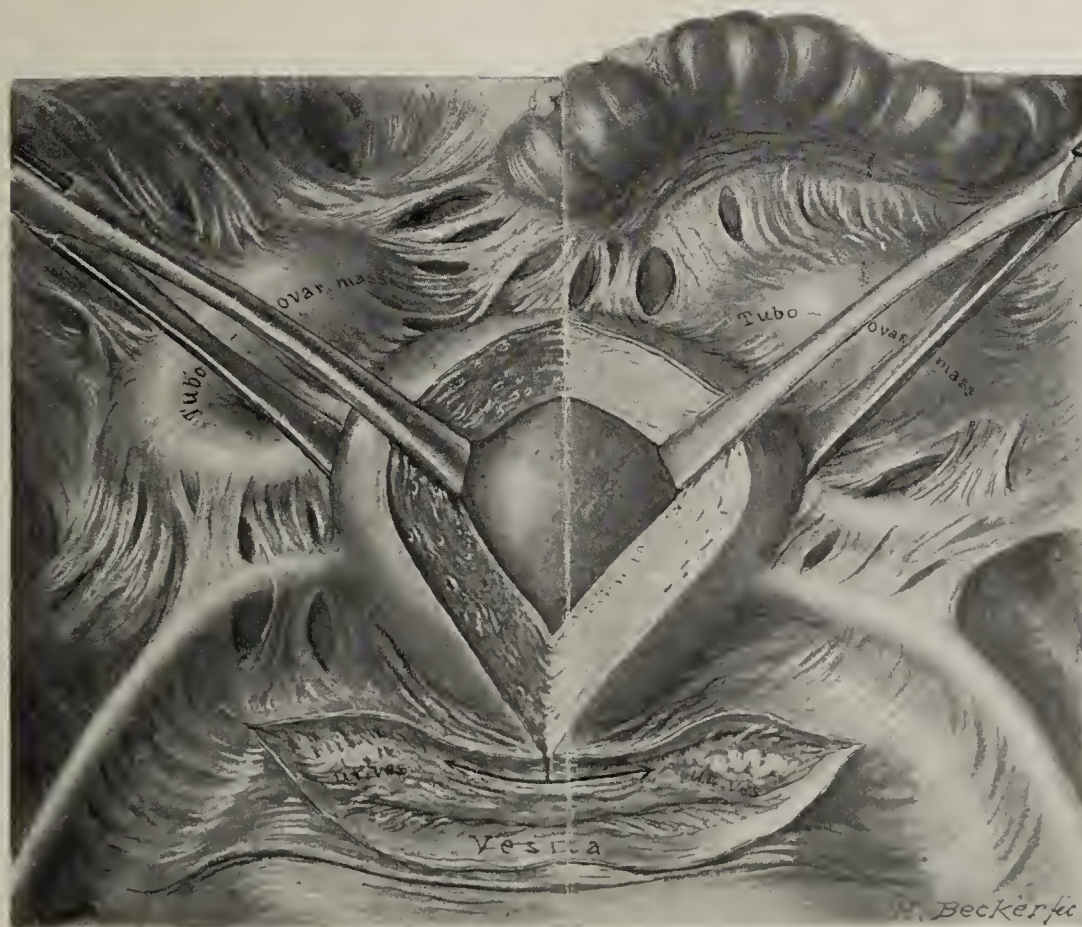


FIG. 4 shows the first step in the bisection of an adherent retroflexed uterus. The forceps catch the anterior face which is opened, then the bladder is pushed down and the cervix divided from side to side as indicated by the arrows.

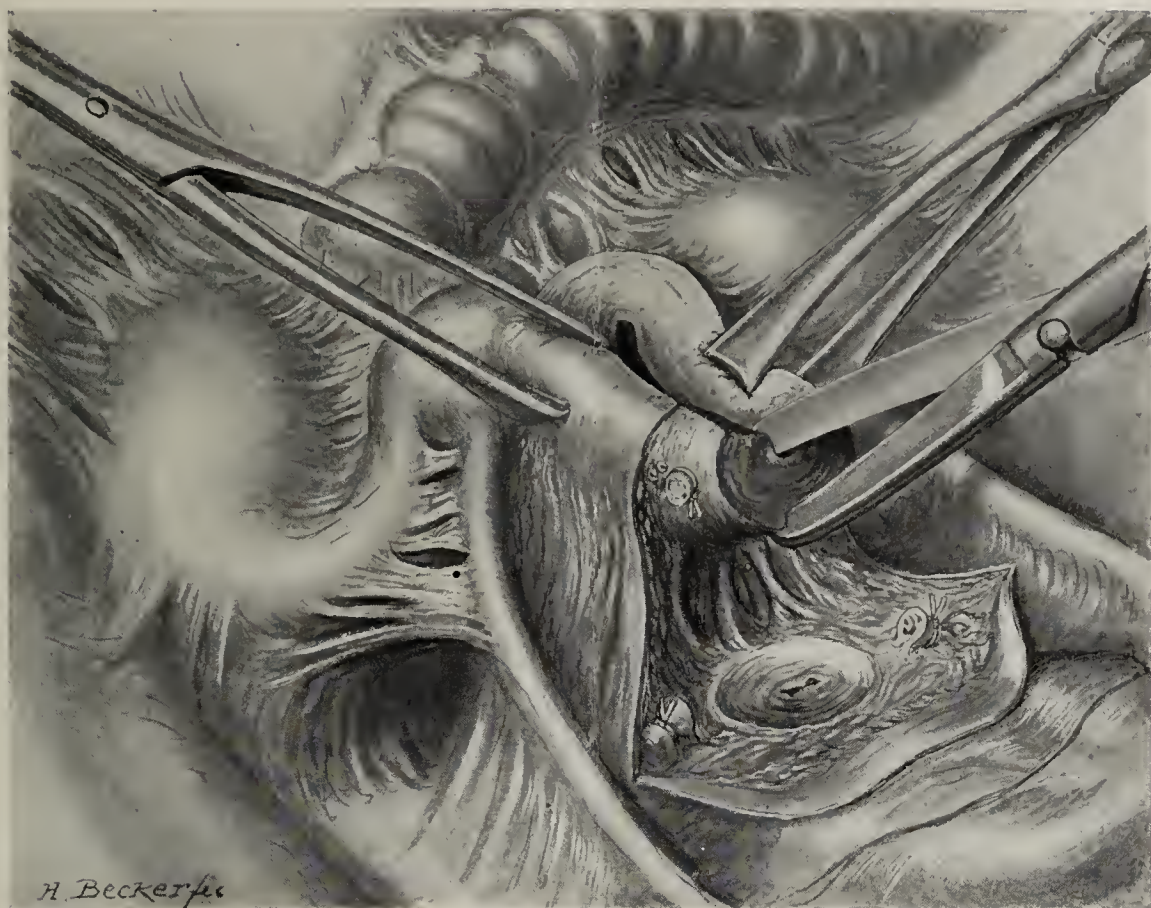


FIG. 5.—After freeing the cervix from its vaginal end it is held up and the bisection completed as shown here, in a direction from below up.

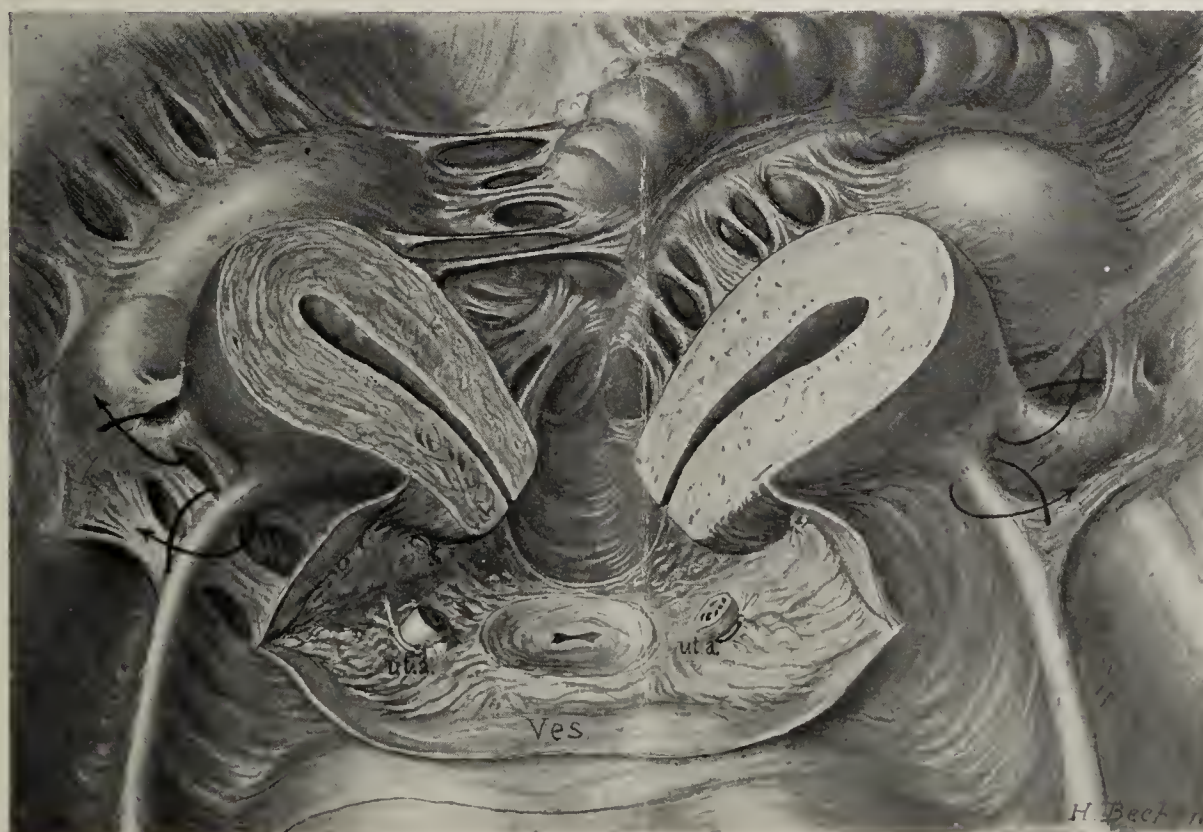


FIG. 6 shows the bisection completed. Each half of the uterus is now removed by applying ligatures as indicated by the arrows on the round ligaments and the uterine cornua. The lateral inflammatory masses are removed last of all.

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and as the uterus is bisected, its cornua are pulled up and drawn apart. With a third pair of forceps the uterus is grasped on one side on its cut surface, as far down in the angle as possible, including both anterior and posterior walls. The museau forceps of the same side is then released and used for grasping the corresponding point on the opposite cut surface, when the remaining museau forceps is removed. In this way two forceps are in constant use at the lowest point. I commonly apply them three or four times in all. As the uterus is pulled up the halves become everted and it is bisected further down into the cervix; if the operator prefers to do a pan-hysterectomy, the bisection is carried all the way down into the vagina. The uterine canal must be followed in the bisection, if necessary using a grooved director to keep it in view. The museau forceps are now made to grasp the uterus well down in the cervical portion, if it is to be a supra-vaginal amputation, and the cervix is divided on one side. As soon as it is severed and the uterine and vaginal ends begin to pull apart, the under surface of the uterine end is caught with a pair of forceps and pulled up and the uterine vessels, which can now be plainly seen, are clamped or tied. As the uterus is pulled still further up, the round ligament is exposed and clamped, then finally a clamp is applied between the cornu of the bisected uterus and the tubo-ovarian mass, and one-half of the uterus is removed. The opposite half of the uterus is also taken away in the same manner.

The pelvis now contains nothing but rectum and bladder, with right and left tubo-ovarian masses plastered to the sides of the pelvis and the broad ligaments, affording abundant room for investigation of their attachments, as well as for deliberate and skillful dissection; the wide exposure of the cellular area over the inferior median and anterior surfaces of the masses, offers the best possible avenue for beginning their detachment and enucleation.

The operator will sometimes find on completing the bisection of the uterus that he can just as well take out each tube and ovary together with its corresponding half of the uterus, reserving for the still more difficult cases, or for a most difficult side, the separate enucleation of the tube and ovary after removal of the uterus.

The operation which I have just described is not recommended to a beginner in surgery; the surgeon who undertakes it must be calm and deliberate, and must bear in mind at each step the anatomical relations of the structures.

The most critical point is the bisection of the cervix and controlling the uterine vessels; if the cervix is slowly and cautiously severed with a steady traction on the uterus under perfect control, there is no danger of seeing the organ suddenly tearing out with rupture of the uterine vessels and frightful hemorrhage. As the divided cervix is pulled apart, the uterine vessels are beautifully exposed and easily caught, only a clumsy operator will plunge his needle or a pair of forceps deep down into the tissues and clamp a ureter. By cutting up the cervix so as to leave a snipe on each side the uterine vessels can be caught at a higher level than that of the division of the cervix.

There is no danger of injuring the bladder, which needs less attention than in any other method of hysterectomy; when the bisection reaches the vesico-uterine fold it may be continued carefully behind this fold well down into the cervix under the bladder which is then easily pushed down as the divided cervix is pulled apart. A simple and a safe way is also to incise the vesico-uterine peritoneum from side to side and push it down with a sponge on a staff and so bare the cervix.

If the uterus is densely adherent to the rectum all the way up to the fundus, a modification of this plan of operating may be followed; the anterior face of the uterus may be bisected and the cervix divided horizontally and the uterine vessels caught, then the rest of the uterus may be carefully divided up its posterior surface in a direction from the cervix towards the fundus. The relations to the rectum are examined as the division is made, and at any point where it seems necessary, a piece of the uterine tissue may be left adherent to the bowel. After the bisection the rest of the enucleation is effected as described above.

I have had abundant opportunity to demonstrate the practical value of this method of treatment in my clinic this year.

In one case (Ward H, 12 April, 1900) the uterus, *tubes and ovaries were so densely adherent* that an effort to free them by the vaginal route failed when I opened the abdomen and caught the uterus by its cornua and bisected it half way down the cervix, and then removed each half uterine body, then with a maximum space under sight and touch the tubes and ovaries were dissected out.

In another instance (W., 5 May, 1900) the entire uterus was bisected and removed and after its removal a large pelvic abscess was extirpated on the right side.

In a case operated upon 7 Nov., 1900 (W., H) the sigmoid on the left and the rectum on the right were the seat of *fistulous openings into the uterine tubes*. Here the fistulae and other complications did not have to be treated until the uterus was divided and brought out into the surface.

Another patient in my private hospital had *tubercular disease of both tubes* (S., April, 1900), which was extirpated with bisection of the uterus.

In one instance (B., 17 Oct., 1900) there were extensive *hematomata of both ovaries* with dense adhesions and a most difficult enucleation was rendered safe by bisection.

In a case of a large *cancerous right ovary* (B., 19 May, 1900), extending into the pelvic cellular tissue, I found a bisection most helpful in clearing out the pelvis and exposing the disease on its median and under sides, and so making possible a much completer enucleation.

The dangers of the method are those of any novel procedure, and must arise for the most part from want of due attention to the details; for example, one can by reckless cutting divide the uterus obliquely so as to cut directly into the broad ligament among the uterine vessels instead of following the uterine canal and making a true coronal section. Again, rashly cutting, one can divide one-half of the cervix and divide the uterine vessels at the same time with frightful hemorrhage; by clamping the bleeding uterine

vessels in an indiscriminate fashion the ureter may be easily included in the clamp.

I suppose, too, that it is easily possible with sufficient carelessness to cut a hole in the bladder.

The risk of sepsis from opening the uterine cavity is practically nil if gauze is packed in around the uterus; furthermore the study of many of these uteri has shown that the infection rarely ever lingers in its cavity.

The advantages of a bisection and enucleation of the uterus as a preliminary to a complete enucleation of uterine tubes and ovaries for pelvic inflammatory and other diseases by the abdominal route are briefly recapitulated:

1. Additional space for handling adherent adnexæ, afforded by the removal of the uterus.
2. Great increase in facility for dealing with intestinal complications.
3. Better access by new avenues from below and in front to adherent lateral structures.

4. Elevation of structures to or above pelvic brim or even out into the abdomen, bringing them within easy reach of manipulation and dissection.

5. The same advantage in approaching both uterine vessels by cutting from cervix out towards the broad ligaments as is secured in approaching one of them in the continuous transverse incision method.

In general, the time of the operation is shortened; its steps are conducted with greater precision; surrounding structures are far less liable to be injured. In this way there are fewer troubles and sequelæ and the mortality is lessened.

I take it that in intraligamentary tumors of both sides this procedure will prove of the utmost advantage in exposing the tumors at a point low down in the loose cellular tissue of the broad ligament.

I have found since writing this that a similar plan of operating has been advocated by J. L. Faure of Paris.

ABSTRACT.¹

THE BACTERIOLOGY OF CYSTITIS, PYELITIS AND PYELONEPHRITIS IN WOMEN.

BY THOMAS R. BROWN, M. D.,

Assistant Physician The Johns Hopkins Hospital Dispensary.

It is only within very recent years that the bacteriological nature of the infections of the urinary tract has been placed upon a firm basis by the work of Rovsing, Melchior, Guyon, Krogius, Schnitzler, Albarran and Hallé and others, and there are still many questions regarding this subject which have not been answered, and various contentions which have not been settled.

The objects of my research have been to determine definitely, as far as lay in my power, the bacterial flora of the infections of the urinary tract in women and to clear up, as far as possible, the moot questions in this subject, to discuss the other factors which may play a part in the etiology of such infections and their relative importance in the development of these conditions, to determine the various modes of entrance of the bacteria into the urinary apparatus, to formulate if possible certain rules regarding the relationship between the species of bacterium found and the clinical picture presented, to suggest from these findings the line of therapy to be carried out, and to note carefully any details in the cases, considered both individually and collectively, that might tend to throw light upon the disputed points of this question or to open up new lines of thought and investigation.

The circumstances attending this investigation were extremely favorable. In the first place, an unusual opportunity was furnished for the study of the etiology of these

infections as most of the acute cases were post-operative and were most carefully studied before, during and after the infection; in the second place, a careful cystoscopic examination was made in all the chronic and most of the acute cases, so that no possible mistake could be made in the diagnosis of the bladder infections; in the third place, the urine was obtained directly from the kidneys by ureteral catheterization in all cases of supposed renal infection, and from the urine so obtained the bacteriological, chemical and microscopical investigations were made.

The cystoscopic examinations were made and the ureteral catheterizations were done by Dr. Kelly, whom I wish to thank sincerely for his unfailing kindness in this particular. This work has been carried on during a space of two years and comprises one hundred cases, besides numerous control experiments.

The complete article will be subdivided into the following sections: I. The method of obtaining the urine aseptically; II. The chemical and microscopical examination of the urine; III. The bacteriological study of the urine; IV. The cases of acute cystitis; V. The cases of chronic cystitis; VI. The cases of tuberculous cystitis which have been considered separately for obvious reasons; VII. The cases with symptoms suggestive of cystitis but with no infection; VIII. The cases of acute pyelitis and pyelonephritis; IX. The cases of chronic pyelitis and pyelonephritis; X. The cases of tuberculous pyelitis and pyelonephritis; XI. A review of the bacteriological, chemical and etiological findings in our series; XII. A short resumé of the work of other investi-

¹ The paper in full will appear in Volume X, The Johns Hopkins Hospital Reports.

gators in this field; XIII. Polymorphism and other peculiarities of the micro-organisms met with in our series, with a few observations on the agglutination of the micro-organisms found in cystitis, pyelitis and pyelonephritis by the serum of the patient, and, XIV. A few therapeutic suggestions directly dependent upon the results of the bacteriological and chemical studies. Under section IV will be found a note on bacteriuria, and under section IX some observations on the relation between calculus and infection.

The number of cases in my series is exactly 100, subdivided as follows: cases of acute cystitis, 26; cases of chronic cystitis, 31 (alone 24, associated with pyelitis 7); cases of tuberculous cystitis, 6 (alone 2, associated with renal tuberculosis 4); cases with symptoms suggestive of cystitis but with no infection, 17 (due to urinary hyperacidity 9, due to other causes 8); cases of acute pyelitis and pyelonephritis, 2; cases of chronic pyelitis and pyelonephritis, 12 (alone 4, associated with cystitis 8); cases of tuberculous pyelitis and pyelonephritis, 6 (alone 2, associated with cystitis 4).

It will be obviously impossible in an abstract as short as this to give more than a very brief summary of the most important findings in the various sections mentioned above.

I. THE METHOD OF OBTAINING THE URINE ASEPTICALLY FROM BLADDER AND KIDNEY.

The following method was employed for obtaining the urine aseptically: From the *bladder*; the vestibule of the vagina and the mouth of the urethra having been carefully cleansed with bichloride of mercury solution (1:1000) or boracic acid solution (saturated) followed by sterile water, the lips of the urethra are pulled apart by traction on the labia and a sterilized glass catheter with a sterilized rubber cuff, about 10 cm. long, on its distal end is introduced, the operator only touching the rubber cuff at about its middle. After the urine has flowed for a short time (so that if a few micro-organisms from the urethra were introduced, they would be washed out by the first-flowing portion of urine), the rubber cuff is withdrawn by traction on its distal end and 10 to 20 ccm. of urine collected in a sterile tube, the cotton plug of which is only removed during the reception of the urine. In obtaining urine from the *kidney*, the sterilized rubber cuff is placed upon the distal end of the sterilized ureteral catheter, which is introduced through a cystoscope into the ureter, great care being taken that it touches nothing in its course until it is inserted into the ureteral orifice. The bladder should be thoroughly washed out just previous to the procedure if there is the least possibility of a vesical infection being present, while if an infection of the bladder has been definitely determined either by urinary or cystoscopic examination, the ureteral orifice should be carefully swabbed off with a solution of nitrate of silver and the catheter inserted but a short way up the ureter (to prevent any possibility of renal infection from the bladder); as in the case before, the urine should be allowed to flow for a short time before the withdrawal of the rubber cuff and the reception of the urine in the sterile test-tube. Ordinarily the urine flows drop by drop but, in case of pyoureter or

hydroureter, or pyonephrosis or hydronephrosis, the urine first flows in a steady stream for a short time until the dilated portion of the ureter or dilated renal pelvis is emptied, when the catheter reaches that portion of the ureteral or renal tract. The adequacy of these methods has been shown by the negative results obtained in 52 control experiments in the case of the bladder and 32 in the case of the kidney.

II. THE CHEMICAL AND MICROSCOPICAL STUDY OF THE URINE.

After having obtained the urine as described above, it is essential that within a very short time (a few minutes if possible) cultures should be made, as well as a careful chemical and microscopical examination either of this specimen or of a larger quantity obtained by catheter at the same time. The *reaction* of the urine should be carefully tested, as by its acidity, neutrality or alkalinity it tells us in a broad way something regarding the nature of the microbe causing the infection. In cases with symptoms of cystitis but with no infection, it is important to determine also the degree of the acidity, which has been done in our cases by titration with a 1-10 normal solution of sodium hydroxide, phenolphthalein being used as the indicator, for, as we shall see later on, urinary hyperacidity may definitely cause symptoms which may easily be mistaken for those of cystitis.

The *specific gravity* of the urine is of importance because of the frequency of low specific gravities in cases of pyelonephritis and also in cases of hysteria and the various neuroses, and its determination is of especial interest when both kidneys are catheterized, as well as the quantitative determination of the *urea*-output from either kidney, so that we may determine the secretory function of each—a question of immense importance when nephrectomy is under consideration.

The determination of the quantity of *albumin* present is of great importance because, combined with a careful cystoscopic examination and a determination of the grade of pyuria and hematuria, it furnishes a valuable criterion for the differentiation between renal and vesical infections, which is of especial value in the hands of those to whom ureteral catheterization is impossible. Of course the urine must be examined shortly after its withdrawal, and considerable experience must have been had in this mode of diagnosis; but, if these requisites have been fulfilled, one may definitely conclude that if the grade of pyuria is decidedly more marked than the grade of albuminuria, cystitis is probably present alone; while, if there is considerable disproportion in the other direction, it speaks for a renal infection, alone or associated with a cystitis. If a person had a chronic nephritis before the development and during the course of the cystitis, the diagnosis would be rendered more difficult, although the presence of casts in this last condition would call our attention to this source of error. Obviously, however, the only absolutely satisfactory method to be employed is catheterization of the ureters combined with a careful cystoscopic examination.

The *microscopical examination* is of value because it tells us of the absence or presence of vesical, ureteral and renal epithelial cells; it calls our attention to the crenation or lack of crenation of the red and white blood-cells (the former of which conditions speaks for a renal hematuria or pyuria if the grade of these conditions is low—if the pyuria or hematuria is of high grade this method of differentiation is of very little value); and it tells us of the morphology, number and motility of the micro-organisms giving rise to the infection. By counting the red and white blood-cells in a definite quantity of mixed urine (1 cmm.) with the Thoma hematocytometer we can definitely determine the success or failure of the mode of treatment employed.

III. THE BACTERIOLOGICAL STUDY OF THE URINE.

The methods of making the cultures and identifying the bacteria found are those usually in vogue, two or three loops of urine or of diluted urine being first plated on agar-agar from which transplantations can be made on the various media. The bacilli should also be counted on the plates so that, by studying the cultures taken from the urine from time to time, the success or failure of the method of treatment employed may be definitely determined.

In all cases, except perhaps acute post-operative cases, the *tubercle bacilli* should be carefully searched for in the sediment, while if there is pyuria or hematuria in an acid urine but with no growth on the ordinary media, intraperitoneal injections into guinea-pigs should also be employed.

In any specimen where the history of the case or the microscopical examination of the sediment makes us suspect the presence of the *gonococcus*, this micro-organism should be sought for by the use of special media and of special staining reactions.

INFECTIONS OF THE BLADDER.

In our series of cases we have divided the cases of cystitis into acute, chronic and tuberculous, and then subdivided these groups along bacteriological lines. We have considered those cases as acute in which the infection has been present but a short time, where there is no *real* contraction of the bladder and where there are no distinct areas of ulceration, while in the chronic cases the duration has been longer, there is practically always more or less ulceration, and the bladder is distinctly and usually markedly contracted.

IV. CASES OF ACUTE CYSTITIS.

These cases are of especial interest because of the fact that, as all but two of the 26 cases studied were post-operative infections, in which the urine had been carefully examined immediately preceding the operation, they furnish us with absolute criteria as to the micro-organisms bringing about the infection and the other etiological factors involved.

In all these cases the micro-organism causing the infection was present in pure culture and generally in large number; in practically all of the cases two and in the rarer ones three or more cultures were made, and in the post-operative cases

a culture was always taken after the disappearance of symptoms; in all these 24 cases the infection entirely disappeared under treatment. The urine in all these acute infections contained varying numbers of pus-cells, red blood-cells and vesical epithelial cells.

The bacteria found in these 26 cases were: *B. coli communis* 15 times, or 57.7 per cent; *staphylococcus pyogenes albus* 5 times, or 19.2 per cent; *staphylococcus pyogenes aureus* twice, or 7.7 per cent, and *B. pyocyaneus*, *B. typhosus* and *B. proteus vulgaris* (of Hauser) once each, or 3.8 per cent, while in one case, microscopically, a colon bacillus was found, although the cultures were not completed.

In all the cases except one—that due to *B. proteus vulgaris* (where the urine was ammoniacal)—the urine was acid, although the degree of acidity varied markedly with the variety of micro-organism, being usually increased in the case of the colon bacillus and typhoid bacillus infections, and diminished in the case of the *staphylococcus* infections, especially in the case of *staphylococcus pyogenes aureus*, where the urine was sometimes neutral in reaction. Especially striking is the prevalence of the colon bacillus and the absolute proof that this micro-organism can by itself give rise to vesical infections as furnished by these studies, while the infections due to the *pyocyaneus* and typhoid bacilli are of great interest, because of their extreme rarity. These last two cases are reported in full elsewhere (*Maryland Medical Journal*, 1900, May; *Medical Record*, 1900, March 10).

The time of the development of the symptoms varied between the 3d and the 20th days after the operation, being shorter in the cases of *B. proteus*, *St. pyogenes aureus* and some of the infections with *B. coli communis*. Apparently the more virulent the micro-organism and the more severe the symptoms, the earlier after the operation the infection manifested itself.

The mode of entrance of the bacteria into the bladder in the majority of these cases was undoubtedly from the urethra by catheterization, although this procedure was performed with extreme care, which is not at all remarkable when we consider Melchior's, Savor's, Gawrowsky's, Bouchard and Charrin's researches upon the bacterial flora of the normal urethra and vulva, colon bacilli and various *staphylococci* being frequently found.

In some cases, however, infection seemed to have taken place definitely from the rectum or from some focus of infection either by means of the blood or lymph currents or by direct transmission.

We were, however, at once struck in considering our cases of acute cystitis by the fact that *other accessory etiological factors* seemed to be absolutely necessary for the production of the infection in the great majority of these cases, which, so to speak, prepared the bladder for the reception of these germs and rendered it susceptible to their usually low pathogenic power.

The most important of these factors, as evidenced by our series, were anemia and malnutrition, constant pressure on the bladder by other organs or by new growths, sagging of the bladder due to relaxation of the perineum, trauma to

the bladder either due to the operation or to the catheterization (these are undoubtedly the most important of these accessory factors, as evidenced by the fact that in almost all the cases of post-operative cystitis the nature of the operation was such that considerable trauma of the bladder was inevitable), the trauma and congestion of the bladder incidental to child-birth, catheterization with poor technique, and a contiguous focus of infection (a large appendicular abscess in one of our cases). In the case of the urea-splitting micro-organisms (*B. proteus vulgaris*), the presence of the bacteria plus the irritation of the ammoniacal urine seems sufficient to bring about a cystitis.

No examples of true vesical *bacteriuria* were met with in our cases, but in a few there was seen a condition nearly approaching this, *i. e.* enormous numbers of bacteria but very few pus-cells in the urine.

V. CASES OF CHRONIC CYSTITIS (non-tuberculous).

The cases varied markedly in duration and in severity; in some cases the symptoms were comparatively slight, in other cases so severe as to render life practically unbearable. Thirty-one cases in all were studied, in 24 of which cystitis alone was present while in 7 a pyelitis was associated with the cystitis. In 3 of these latter cases the pyelitis had preceded the cystitis and in 4 the reverse had taken place; in all the first 3 the vesical symptoms were very slight. In this series of 31 cases *B. coli communis* was met with 16 times, or 55.2 per cent (15 times in pure culture, once in association with the tubercle bacillus); *St. pyogenes aureus* 3 times; or 10.3 per cent; *St. pyogenes albus* twice, or 6.9 per cent; a slowly liquefying (gelatin) urea-decomposing white staphylococcus 4 times, or 13.8 per cent, and *B. proteus vulgaris* once, or 3.4 per cent. With the exception of the one case mentioned (*B. coli* and *B. tuberculosi*), the micro-organisms were always present in pure culture. Of the 31 cases, the urine was acid in 26 (occasionally neutral or exceptionally slightly alkaline in some of the staphylococcus infections), alkaline or ammoniacal in 5 (*B. proteus vulgaris*, slowly-liquefying urea-decomposing white staphylococcus), although in some of these latter cases, when the bladder infection is very slight and the renal infection marked, the urine may be neutral or even acid.

The common *modes of infection* seemed to have been from the vulva or urethra usually by catheterization, from the rectum, from the kidney, from poor technique in examining or treating the bladder. The *other factors in the etiology* of the condition were practically the same as in our series of cases of acute cystitis; a new accessory etiological factor is to be found in this series in operations upon the urethra.

VI. TUBERCULOUS CYSTITIS.

Six cases of tuberculous cystitis were met with in our series. In one case and possibly in another, the cystitis occurred alone; in the other cases it was associated with a tuberculous pyelitis or pyelonephritis. Five of the cases were chronic; one was comparatively acute. The constitutional symptoms and the vesical lesions were marked in all

these cases but one. In all, tubercle bacilli were found, usually in small numbers, occasionally in comparatively large numbers. They were present in pure culture in all but one case, where the colon bacillus was also present (secondary infection after a suprapubic cystotomy). The urine was always markedly acid and contained usually a large number of pus and red blood-cells, the latter being comparatively more frequent than in the other cases of chronic cystitis. The *mode of entrance* of the bacilli was difficult to determine; the bladder seemed to be affected first, probably by metastasis from some tuberculous focus elsewhere in the body. *Other etiological factors* were difficult to determine; only one case gave a family history of tuberculosis and only one showed a pulmonary lesion; in some cases weakness, anemia and malnutrition seemed to have rendered the bladder susceptible to the infection. In some cases the onset was gradual and insidious, in other cases the symptoms of onset were those of a typical acute cystitis.

VII. CASES WITH SYMPTOMS OF CYSTITIS BUT WITH NO INFECTION.

Besides the increased frequency of urination, burning sensation, etc., seen after the use of various drugs and in certain neurotic conditions, we have met with two classes of cases with symptoms of cystitis but with no infection. The first class is of especial interest, the symptoms being due to *urinary hyperacidity*, which was determined by titrating 10 ccm. of freshly drawn urine with one-tenth normal sodium hydroxide solution, phenol-phthalein being used as the indicator. Nine such cases were met with and the acidity of the urine varied from twice to five times the normal. The urine always contained a few and in the more severe cases a moderate number of pus and red blood-cells, while cystoscopic examination usually revealed a markedly ingested trigonum. The condition seems to be one of the manifestations of a general neurosis which requires general as well as local treatment, the latter of which consists mainly in the neutralization of the intense acidity of the urine by the administration of alkalis by mouth. Cultures of the urine were always negative and the condition, so far as I know, has not definitely been described previously. The condition is of especial importance because, if misinterpreted, local applications, irrigations, etc., are frequently inaugurated which, in the hands of all but the most careful and skillful, frequently lead to vesical infections.

Eight cases with symptoms of cystitis but with no infection are reported due to other causes; such causes are relaxation of the vaginal outlet, especially if marked anteriorly, retroflexed uterus, pelvic inflammatory disease with vesical adhesions, large pelvic neoplasms pressing upon the bladder, mucous polypi protruding from the vagina, and varicosity of the vesical veins. If the pathological condition is corrected by operation, the vesical symptoms shortly disappear.

PYELITIS AND PYELONEPHRITIS.

These studies are unique in that the urine from which they have been made was obtained directly from the kidney by

ureteral catheterization. Both kidneys were usually catheterized, so that the two sides could be compared—a most important point in determining upon the advisability or non-advisability of nephrectomy.

VIII. ACUTE PYELITIS AND PYELONEPHRITIS.

Only two cases were met with, in both of which the renal infection was secondary to the bladder infection. One was due to *B. coli communis* and the urine was acid; the other was due to *B. proteus vulgaris*, and the urine was alkaline. In either case the other kidney was perfectly normal. It was interesting to note that in one of these cases the affected kidney was the one suspended at the operation.

IX. CHRONIC PYELITIS AND PYELONEPHRITIS (non-tuberculous).

Twelve cases of this condition were studied, in 4 of which the pyelitis was present alone, in 8 associated with cystitis. Catheterization of both kidneys showed that the infection was unilateral in all but one case. The symptoms were very variable, being sometimes almost nil, sometimes very severe. The urine from the infected kidney was usually pale, of less specific gravity, increased in amount, low in urea percentage and contained a greater or less number of pus-cells, some red blood-cells and ureteral or renal epithelial cells. The bacteria found in these 12 cases were: *B. coli communis* 6 times, or 50 per cent; *B. proteus vulgaris* 3 times, or 25 per cent; the slowly-liquefying, urea-decomposing white staphylococcus twice, or 16.7 per cent, while in one case there was no growth, the infection evidently having died out. The urine was acid in the colon bacillus cases, alkaline in the cases due to the other micro-organisms. As to the *mode* of infection, in 5 the bladder was infected first and the kidney secondarily, evidently by an ascending ureteral infection, while in 5 and probably in one other the kidney was infected first; that is, the infection was probably carried directly to the kidney by means of the blood or lymph currents; in one case the infection was an ascending ureteral infection, there being a uretero-vaginal fistula.

An interesting point regarding the *relation between infection and calculus formation* was to be made out from a study of these cases. In all 5 cases of chronic pyelitis, where the urine was alkaline due to a urea-decomposing micro-organism, a renal calculus composed of phosphates and carbonates of calcium and magnesium was found, while from the centre of one of the calculi a pure culture of the micro-organism causing the pyelitis was obtained.

X. THE CASES OF TUBERCULOUS PYELITIS AND PYELONEPHRITIS.

Six cases of this nature were met with, in 2 of which the renal infection occurred alone, while in the other 4 a vesical infection was associated with it. One of the cases was an acute infection, while 5 were chronic. All cases were pure infections and in all 6 the tubercle bacilli were found in the urine. The urine was always acid, contained considerable albumin, many pus-cells, more red blood-cells

than seen in the other forms of pyelitis, and renal and ureteral epithelial cells. None of the 6 cases gave a tuberculous family history and only one showed a tuberculous lesion outside the urinary tract. In 4 of the cases the kidney seemed to have become infected from the bladder by an ascending ureteral infection.

In the complete article, section XI is devoted to a general consideration of the results obtained, and section XII to a discussion of the bacteriological results obtained by other observers.

Section XIII treats (1) of the polymorphism of various bacteria, especially as regards variation in cultural peculiarities, motility and virulence of the colon bacilli and the chromogenic properties of the staphylococci, and (2) of the agglutination of the bacteria by the patient's serum in cystitis and pyelitis, a positive reaction being obtained in 2 of the 3 cases tested.

Section XIV deals with a few therapeutic suggestions directly dependent upon the bacteriological findings, the question of treatment not being further discussed in this article, as it obviously belongs more to the surgeon than to the bacteriologist. To render the urine a poorer medium for the growth of bacteria and to help to wash out the bacteria, pus-cells, etc., present, large quantities of water should be administered, preferably by mouth, but if this is not feasible, by rectal enemata or by subcutaneous injections. The administration of substances which render the urine somewhat antiseptic, as urotropin, cystogen, salol, etc., is advisable, especially in the acute cases. Also in cases associated with an alkaline urine, acids such as boracic, benzoic or camphoric acids should be given by mouth in sufficient quantity to render the urine acid, while in the acid infections alkalis should be given until the urine is alkaline, as it would seem probable that by these means we diminish the growth of the respective micro-organisms by furnishing a less favorable medium. The same condition of inhibition of growth would probably be brought about in any case by the administration of a great excess of either acid or alkali. It is essential that the resisting power of the patient be increased as far as possible by a careful attention to all questions of personal hygiene, the insistence upon plenty of fresh air, sunshine and good food, the removal of depressing or very exciting influences, the attention to any disorders of the blood, the circulatory and respiratory organs or the organs of digestion and elimination if such conditions are present. Of course, in many cases other measures besides the ones just mentioned have to be employed, such as topical treatment, irrigations, instillations (nitrate of silver has proven of most value to us in these connections), operative treatment of various kinds, etc., and the above are but the suggestions regarding the general medical treatment of cases of cystitis, pyelitis and pyelonephritis derived directly from the bacteriological study of the cases.

DISCUSSION.

DR. YOUNG.—I have enjoyed this paper and I think Dr. Brown is to be congratulated for his excellent work. My

interest in this subject has extended over several years, as I have been working, particularly on male subjects, during that time along the same line. In looking over the results obtained I was struck by the great dissimilarity of the organisms we have found. My work includes, I think, three or four times as many organisms as have been found in the cases studied among the females. For instance, among others I found all forms of the proteus, the streptococcus, the staphylococcus albus and the aureus, the bacillus lactis aërogenes, and, several times, the gonococcus.

Another discrepancy between our results is that the colon bacillus, which occurred in the great majority of cases in the female, was not so often found in the male. The staphylococcus pyogenes albus in my cases was found to be a much more common cause in the male of acute or chronic cystitis and nephritis.

One particularly interesting point in the paper is in regard to the effect of these bacteria upon the urine, as Dr. Brown has mentioned. For instance, in my cases with a pure colon bacillus infection there was always an acid reaction, while with the proteus there was a marked alkaline or ammoniacal reaction. If both were present in the same case there was usually only a slight alkalinity, the acid-forming colon bacillus apparently neutralizing more or less completely the alkalizing effect of the proteus group. In one case I was able to prognosticate the presence of these two organisms simply upon the finding of a very slightly alkaline urine with the presence of large numbers of bacilli—enough to have made it strongly acid if colon alone were present, and very alkaline if proteus were the sole organism.

We have encountered a number of staphylococci that could not exactly be classified; in fact, there were all grades of staphylococci in the cultures I have examined, some requiring 15 days to liquefy gelatin and some that did not liquefy it at all, and I suspect that Dr. Brown's staphylococci belong to the group that Melchior has called the diplococcus ureæ non-liquefaciens.

As to the amount of albumin in making a diagnosis of pyelitis from cystitis, I think from practical experience it is often pretty difficult to determine. Finger, discussing the question of infection of the pelvis of the kidney after gonorrhœa, says that if the albumin has reached 1.5 per cent you can generally safely consider that the pelvis of the kidney is involved, but we have noticed in examinations of the urine in cases of cystitis the amount of albumin varied very greatly, sometimes being present in considerable amount, sometimes entirely absent, with similar amounts of pus present.

Dr. Brown's case of typhoid infection of the bladder is certainly a very interesting one. In the first place, the organism was introduced from without; and, secondly, it is the only case I believe in which a careful cystoscopic study has been made in an acute cystitis due to the bacillus typhosus. The symptoms in his case were very severe and differ in that respect from the usual cystitides following typhoid fever. In a great majority of cases in which the

bacillus appears in urine after typhoid fever there is no irritation at all. It seems to be the fact that infection of the bladder by the typhoid bacillus is a very mild one in most cases, but I have recently had a case of severe chronic cystitis, with marked ulceration of the mucosa, in which the bacillus typhosus was the sole infecting bacterium, and that seven years after the attack of typhoid fever.

In all the cases infected with the proteus I have had the urine has been strongly alkaline, but we have recently had one case in the hospital that had an acid reaction, and a study of the organism by Dr. Sabin showed it to be the proteus Zenkeri, which is not as pronounced in its effect upon media and is not an alkalizer; if inoculated into sterile urine it renders it acid. This is interesting in that bacteriologists, I believe, consider all the proteus organisms to belong to one group and to be interchangeable.

Gonococcus infections of the bladder were not present in Dr. Brown's cases, and I believe they are much more common in the male, owing to the greater severity of the urethral inflammation in the latter. Thus I have found this organism six times in the bladder, in three acute and three chronic cases of cystitis. The only other cases in the literature, however, where cultivations of the gonococcus were obtained, were in the female, the difficulty of obtaining cultures from the bladder of the male in acute gonorrhœal infections being the probable cause. This was overcome in my cases by aspiration of the bladder above the symphysis.

The demonstration of the ease with which the bladder may be aspirated for cultures will probably soon increase the present limited number of observations on the ability of the gonococcus to invade the bladder.

DR. WELCH.—There are only one or two points which I shall undertake to discuss in Dr. Brown's very interesting and important paper. I am impressed by the fact that both Dr. Brown and Dr. Young find that bacteria which have ordinarily very limited pathogenic activity and do little harm elsewhere in the body are so often concerned in cystitis and pyelitis. This is the more remarkable as it has been demonstrated that the healthy bladder is capable of disposing of large numbers of much more virulent kinds of bacteria. The slowly-liquefying and the non-liquefying white staphylococci we are accustomed to regard as among the least pathogenic pyogenic cocci, and still these are apparently often present in the urine in cystitis and are interpreted as the exciting factors in the causation. This should in my opinion lead us to attach much importance to various accessory causes which render the urinary passages incapable of resisting even these mildly pathogenic bacteria, and it would be a one-sided view which failed to take into consideration in the etiology of cystitis and pyelitis the non-bacterial factors.

The question has been raised as to the identity of the non-liquefying white staphylococcus. I should like to inquire whether the coccus in question may not be Staphylococcus cereus albus. There is every gradation among the pyogenic staphylococci as regards such properties as rapidity

and intensity and tint of color-production, liquefaction of gelatin, coagulation of milk and virulence when tested on animals, so that there is much in favor of the view that they are varieties of a common species. We have been in the habit of designating as *Staphylococcus epidermidis albus* the slowly liquefying and slowly coagulating white staphylococcus, which, moreover, is of limited virulence and, as has been abundantly demonstrated, is a regular inhabitant of the human epidermis. I should infer from Dr. Brown's description that this *Staphylococcus epidermidis albus* has been often encountered by him in cases of cystitis.

DR. HUNNER.—I have been struck with the apparent non-relationship between the degree of bladder disease and the infecting organism which under other conditions is often very virulent. Especially is this true in my experience with the streptococcus.

We had a case in Dr. Kelly's service last fall who was the wife of a physician and had been under careful observation. Eight weeks before admission her first sign or symptom of disease appeared in the form of a marked hematuria, the urine being of a claret color and occasionally containing small bright red clots. After three weeks she became anemic, had occasional pains in the right kidney region, and experienced some headache, giddiness, and nausea. There had been no elevation of temperature until two weeks before admission, when she was suddenly taken with a severe shaking chill which lasted one and one-half hours and was followed by a rise of temperature to 104.3° F., violent headache, pains in the legs, retching, vomiting, and great restlessness. The temperature gradually subsided but had reached 100° every afternoon since. The urine was found to contain great numbers of streptococci in pure culture, and a catheterized specimen from the right kidney showed infection by the same organism. Nephrectomy was done and a small stone was found in one calyx with multiple foci of necrosis scat-

tered throughout the kidney. The bladder mucosa seemed entirely healthy.

A patient was admitted this spring who had suffered with symptoms of stone in one kidney for the past two years, and in both kidneys for three months past. Streptococci were obtained in pure culture from the bladder and from either kidney, but the bladder mucosa showed no lesion. Wax-tipped bougies were scratched by stone in either kidney.

A case came in a day or two ago and from her history stone in the right kidney was suspected. On catheterization of the bladder macroscopically, clear urine was obtained. Cystoscopy revealed a healthy-looking bladder. I catheterized the right kidney with a wax-tipped bougie and obtained scratch-marks from stone. On examination of my plates to-day I was surprised to find a pure growth of streptococcus both from the bladder and the right kidney.

DR. BROWN.—I would like to say that one of the probable reasons why the bacterial flora in my cases is not so large as in Dr. Young's experience is that my cases were taken entirely from private patients where the chances of infection are decidedly less.

In regard to the disputed staphylococcus, I thought, of course, that it possibly was identical with the diplococcus of Melchior but could not convince myself of it, as it certainly showed no especial tendency to assume the diplococcal arrangement.

As I have stated before, the infections were almost always confined to those cases in which the resistance was very low, or the traumatism of the bladder was marked.

I have not attempted to carefully differentiate the various white staphylococci found in these cases, for it seems almost impossible to satisfactorily separate these micro-organisms into especial groups, as all gradations in cultural peculiarities were met with. As Dr. Welch has stated, some of them certainly could be best considered as *Staphylococci epidermidis albi*.

THE INTRINSIC BLOOD-VESSELS OF THE KIDNEY AND THEIR SIGNIFICANCE IN NEPHROTOMY.

BY MAX BRÖDEL.

[PRELIMINARY COMMUNICATION.¹]

In view of the enormous number of investigations of the different structures of the kidney recorded in the literature

¹ Since this article was sent to press, I learned that Dr. William Keiller, of Galveston, Texas, has been following a similar line of research. His findings were embodied in a report to the Texas State Med. Soc., in whose Transactions for 1900 they appear. I have just received through the kindness of Dr. Keiller some of his specimens which substantiate many of the points brought forth in this paper, although the methods he employed differed essentially from mine. This being merely a preliminary communication precludes the possibility of discussing in detail Dr. Keiller's excellent work.

it seems strange that only scanty information exists on the actual course of the larger blood-vessels and their relation to the pelvis of the kidney. The normal and abnormal arrangement of the vessels at the hilum are well known and the microscopical pictures of the vessels in the cortex and pyramids are likewise thoroughly familiar to every student. But as to the actual form of the pelvis and the course and distribution of the larger vessels around its walls very vague ideas still prevail. It is evident that exact knowledge of the anatomy of this region would prove of the utmost im-

portance to the surgeon in enabling him to open the pelvis of the kidney without running the risk of cutting large branches of the renal artery.

In order to study this region I made a large number (40) of celloidin injections of human kidneys. The injected specimens were then digested² and the casts thus obtained, examined. Nearly thirty additional injected kidneys were not digested, but were cut into sections in various planes in order to control the results obtained by the method of digestion. Some of these sections were rendered translucent by the usual methods.

I made separate injections of the arteries, of the venous system and of the pelvis, combinations of any two out of three and finally triple injections. The great majority were of the last class. At first I confined my injections to kidneys which seemed normal so far as regarded form and size; later, after I had, in this way, determined the law according to which the vessels were grouped, I concentrated my attention upon abnormally shaped kidneys. The present paper will contain a short abstract of the main results of these studies. I shall confine myself to the description of the normal form and mention briefly only a few variations. A more elaborate communication will appear later.

The Pelvis of the Kidney.—From a surgical standpoint all forms of pelves may be classified under two main groups.

(1) True pelves with major and minor calices.

(2) Divided pelves, where there is no free communication possible between all of the calices inside of the kidney.

(1) *True Pelves.*—Fig. 1 shows the ideal form of a true pelvis. There are eight calices; the uppermost (1) and lowest (8) of which may have double papillæ. The remaining six calices stand upon the pelvis in a double row; an anterior, irregularly arranged (2, 4, 6) and a posterior, more regular, row (3, 5, 7).

The horizontal axis of the pelvis (Fig. 1 D, *a*, *a'*) runs from the posterior surface of the kidney obliquely through the organ to the outer third of its anterior surface and the two rows of calices leave this axis at almost equal angles. The posterior calices, therefore, point to a line just a little posterior to the lateral convex border of the kidney (*b*), while the anterior calices are directed straight forward into the convex anterior region of the organ (*c*). This form of the pelvis is, next to the distended pelvis, the most favorable for a surgical incision.

² I employed Schieferdecker's corrosion-method, slightly modified by Mixter and Mall. The procedure was as follows: The vessels and pelvis of the kidney were thoroughly washed out and then dehydrated with alcohol and ether. The arteries, veins and pelvis were then injected with cinnabar, Prussian blue and arsenic preparations of an alcohol and ether solution of celloidin, respectively. The kidney was then placed in a digesting fluid consisting of varying amounts of 1:3000 pepsin (Sharp & Dohme) dissolved in 0.3 per cent to 0.5 per cent of HCl. The process of digestion was completed in from three or four days to two weeks. When the substantia propria and the connective tissue of the kidney were completely dissolved, they were washed out with a gentle stream of water, leaving only the casts of the injected vessels and pelvis. The casts were preserved in glycerin to which a few drops of carbolic acid were added.

The great majority of pelves have well defined major calices, with a very narrow lumen, and owing to this condition it is often impossible to gain access to the minor calices and remote pockets through a surgical incision into the pelvis at the site of the hilum. Furthermore, this incision must be short, as there is a constant branch of the renal artery running downward over the posterior surface of the pelvis at the hilum.

The varieties of the ideal form are very numerous and will be described in detail in the fuller communication above referred to. All kidneys with a true pelvis have a smooth surface or moderate degree of lobulation, regular outline and, as a rule, a normal blood-supply.

(2) *Divided Pelves.*—Fig. 2 shows the typical form of a divided pelvis. Comparing it with Fig. 1 one finds that between calices 2, 3 and 4, 5 there is a zone of cortical substance (*a*), which extends to the hilum. It divides the upper part of the pelvis from the lower, and in the majority of cases the lower portion receives the greater number of calices. Although the number of calices in divided pelves may be eight, they are generally more numerous. In other respects the topography of these pelves is similar to that of the true pelves. A kidney with a divided pelvis, as a rule, preserves its foetal lobulations and has an abnormal arterial circulation; the division between the individual sections of the pelvis is generally marked on the surface by an especially deep groove, thus causing the appearance as though there were two separate kidneys, one on top of the other. Frequently they are indeed separate organs as far as their secretory function and their arterial circulation are concerned. The veins, however, collect, as a rule, in one single trunk. These conditions are readily understood by one who is familiar with the different stages of the development of the kidney, with its origin, its ascent from the pelvis to the lumbar region and finally the wandering in of the vessels.

The Renal Artery.—The renal artery divides at the hilum, as a rule, into four to five branches, the distribution of which, in relation to the pelvis, is such that three-fourths of the blood-supply is carried anteriorly, while one-fourth runs posteriorly. The relative size of the two systems may occasionally be $\frac{4}{5}:\frac{1}{5}$, $\frac{2}{3}:\frac{1}{3}$, but rarely $\frac{1}{2}:\frac{1}{2}$. The arteries are end-arteries in the strictest sense of the word and the branches of the anterior division never cross over to the posterior side, or *vice versa*. They do not anastomose with each other.³ The plane of division between the two arterial trees is indicated by the axes of the posterior row of calices (see Fig. 1 D *b* and Fig. 3 B arrow).

Fig. 3 B demonstrates this in a schematic way. The sec-

³ To Hyrtl apparently is due the credit of having first mentioned the "natürliche Theilbarkeit der Niere," by which he means that in a corrosive specimen the two arterial systems are completely separated by the pelvis. He also affirms that this arrangement of the renal arteries is found "without exception in all mammalia from the whale to man." [Hyrtl, *Topographische Anatomie*. Wien, 1882. Bd. I, pg. 834.] Hyrtl's statement has unfortunately been overlooked and up to this date the text-books on anatomy and surgery make no mention of this anatomical fact, so important to the surgeon.

tion is imagined as passing transversely through the middle of the kidney, as in the lower diagram in Fig. 1. The artery (*a*) sends a large branch (*a'*) anteriorly and a small branch (*a''*) posteriorly. Both branches are seen running close to the pelvis and the calices up to the region of the papillæ, whence they send off fan-like branches (*b*) around the pyramids. The anterior branch (*a'*) supplies the whole of the anterior pyramid (*P*) and the anterior portion of the posterior pyramid (*P'*), while the posterior branch (*a''*) supplies only the remaining portion of the posterior pyramid (*P'*). The arrow indicates the division between the two vascular trees. *c* represents a section of the long lateral column of cortical substance, which is situated between the anterior and posterior rows of pyramids *P* and *P'*.

The greater part of the arterial circulation of the kidney follows this system. The entire region from calices 2 to 7 has this arrangement. Around the uppermost (1) and lowest (8) calyx, however, the arteries have a somewhat different arrangement (Fig. 4). They are derived from the anterior group of vessels and run either as a single trunk, having a diameter of 2-3 mm., to the base of the major calyx, or divide before they reach the calyx into three branches, I, II, III. Branch I and branch III run courses similar to those of branches *a'* and *a''* in Fig. 3 B, *i. e.* anteriorly and posteriorly to the calyx. It is obvious that their arrangement must prolong the arterial division, existing in the central portion of the kidney, upward and downward. Branch II may be short, as in Fig. 3 A (upper pole), and vessels coming from branches I and III partially may take its place. Or it may be of considerable length, as in Fig. 5, where it makes a long sweep around the inner border of the pole. Branch II is the one that generally plays the rôle of the supernumerary artery; it may arise from the renal artery near its aortic origin (Fig. 5 *a* and *b*) or even from the aorta (Fig. 5 *c*); in the latter case it must be considered a supernumerary artery.

Although separate arteries are found in kidneys with smooth surfaces, they are much more frequently met with in those that have preserved their foetal lobulation. This abnormal arrangement of the arteries is, perhaps, the cause of the persistence of the lobulated form. When he meets with a kidney having a distinctly lobulated form, the operator may expect to find a long hilum with separate arteries and an abnormal renal pelvis.

The further course of the arteries, the irregularities that may occur and to what extent they affect the above described schema, will be dealt with in a fuller communication.

The Renal Vein.—Concerning the veins, I shall here record only a few notes dealing with their more important characteristics.

While there is a complete arterial division in the plane connecting the posterior calices and terminating in the lateral half of the upper and lower calices, the veins follow quite a different arrangement. Around the bases of the pyramids they anastomose and form the familiar venous arches. They unite in large branches that run between the sides of the pyramids and the columns of Bertini to the necks of the calices, where they lie between the pyramid and

the arterial branches. The thickness of these collecting veins accounts for the peculiar lobulated appearance of the base and sides of the pyramids (Fig. 6 B). Around the necks of the calices, both anteriorly and posteriorly, these veins form a second system of anastomoses (Fig. 6 B *b*) much shorter and thicker than that at the base of the pyramids (*a*). This appears as a number of thick loops or rings which fit like a collar around the necks of the calices. Nearly all the collected blood of the posterior region is carried anteriorly through these short thick stems, to join that of the anterior portion at the point indicated by *c*.

In comparing Figs. 3 and 6 one finds that an incision through the posterior row of calices would avoid all the arteries but would sever six of these collecting veins. As there remain, however, sufficient anastomoses at the upper and lower pole of the kidney, no serious consequence should follow an injury to these veins. The large veins at the hilum are generally described as being in front of the artery. This is, however, only the case in the neighborhood of the vena cava, while at the hilum and throughout the entire kidney the veins are usually situated between the arteries and the pelvis.

The Surface of the Kidney and its Relation to the Underlying Structures.—If one is thoroughly familiar with the kidney's surface it is a comparatively easy matter to determine the arrangement of the underlying structures; one can map out fairly accurately the position of the pyramids, of the columns of Bertini and of the calices; and as a consequence the position of the plane of arterial division can also be determined. Let us consider briefly the principal landmarks.

The anterior surface (Fig. 7 B) of a normally shaped kidney is convex and has its greatest prominence at the lower portion at the point indicated by *a*. The posterior surface (A) is somewhat flattened. A lateral view of the organ (C) shows this very clearly; there is also rendered visible a depression (*b b'*), which indicates the position of the lateral column above referred to, or the line of division between the anterior and posterior rows of pyramids. This depression, however, by no means indicates the division between the arterial systems, as below it is situated the greatest number of large vessels contained in the kidney. This line (*b b'*) is therefore a most important landmark and in every nephrotomy should be thoroughly mapped out. The other depressions on the surface indicate the positions of the margins of the individual pyramids or subdivisions of such.

Fig. 8 shows the same kidney as Fig. 7, with its pyramids and calices schematically drawn. The posterior pyramids (A 3, 5, 7) are long and slender, while the anterior ones (B 2, 4, 6) are more rounded at their base, thicker and do not extend so far laterally as the posterior pyramids. Consequently, the line of division (*D b* and *b'*) between the pyramids leans more towards the anterior surface of the kidney, so that the anterior surface of the organ bulges, while the posterior is flat.

Between the pyramids are the columns of Bertini which carry the larger vessels. Fig. 8 C shows that these columns join in a longitudinal column (*b b'*), in which all of the largest

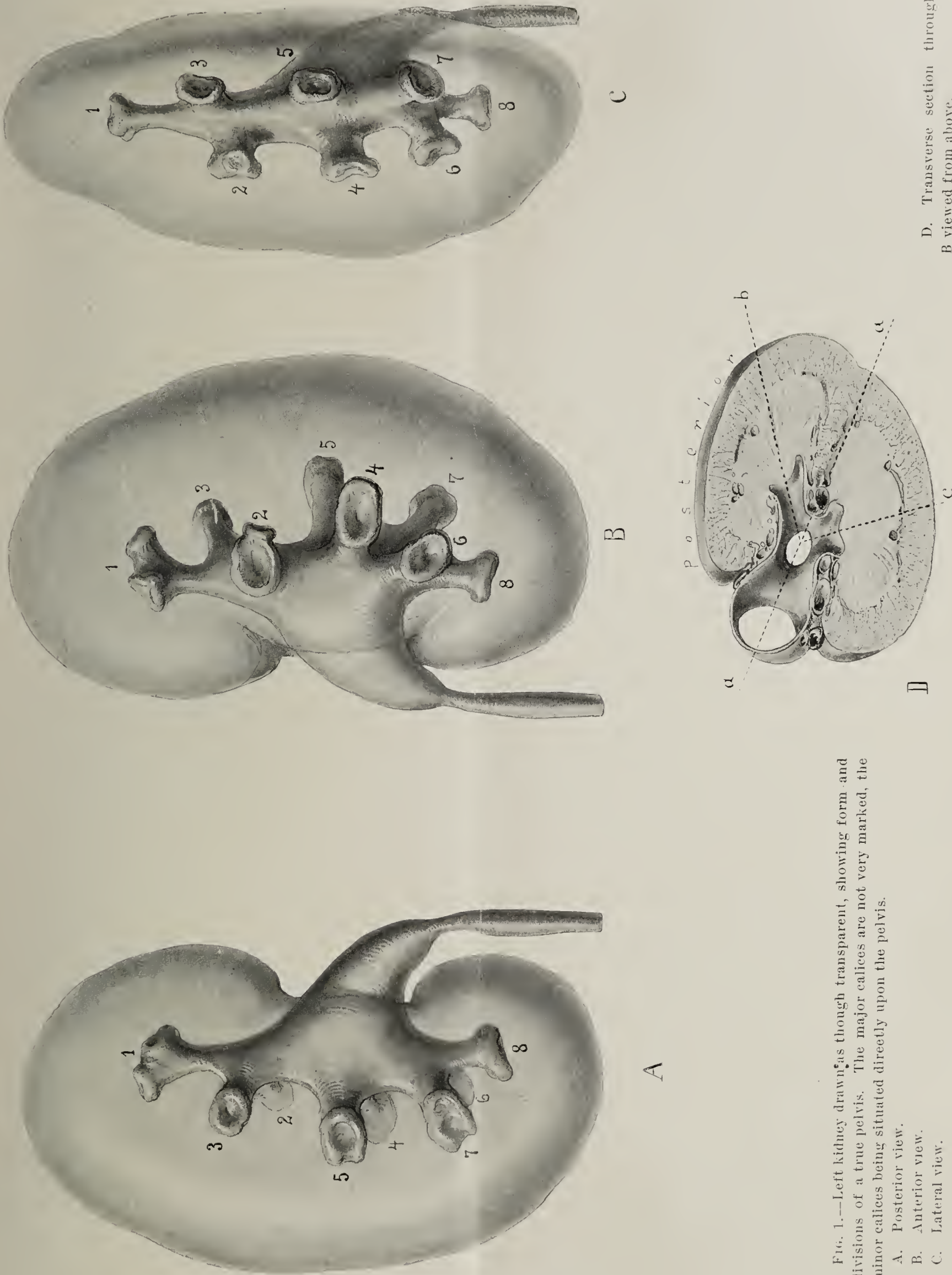


FIG. 1.—Left kidney drawn as though transparent, showing form and divisions of a true pelvis. The major calices are not very marked, the minor calices being situated directly upon the pelvis.

A. Posterior view.

B. Anterior view.

C. Lateral view.

D. Transverse section through B viewed from above.

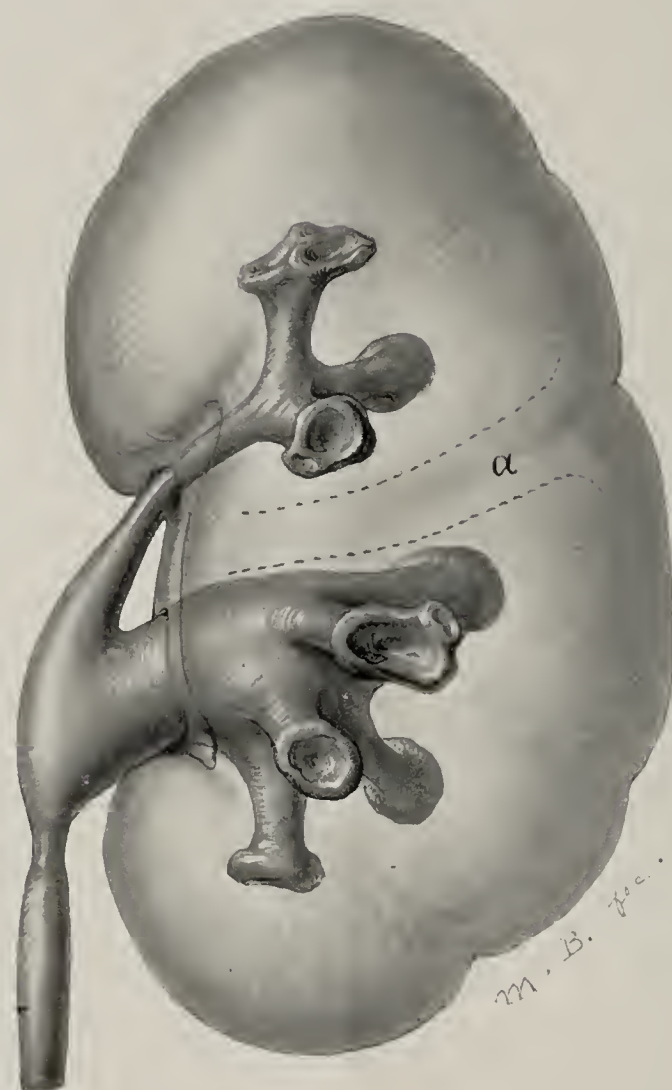


FIG. 2.—Left kidney with typical form of a divided pelvis. The two divisions of the pelvis are separated by an area of cortical substance (α) extending almost to the hilum. As a rule the upper division is narrow and has fewer calices than the lower. The division between the two branches of the pelvis is generally marked on the surface of the kidney by a deep depression.

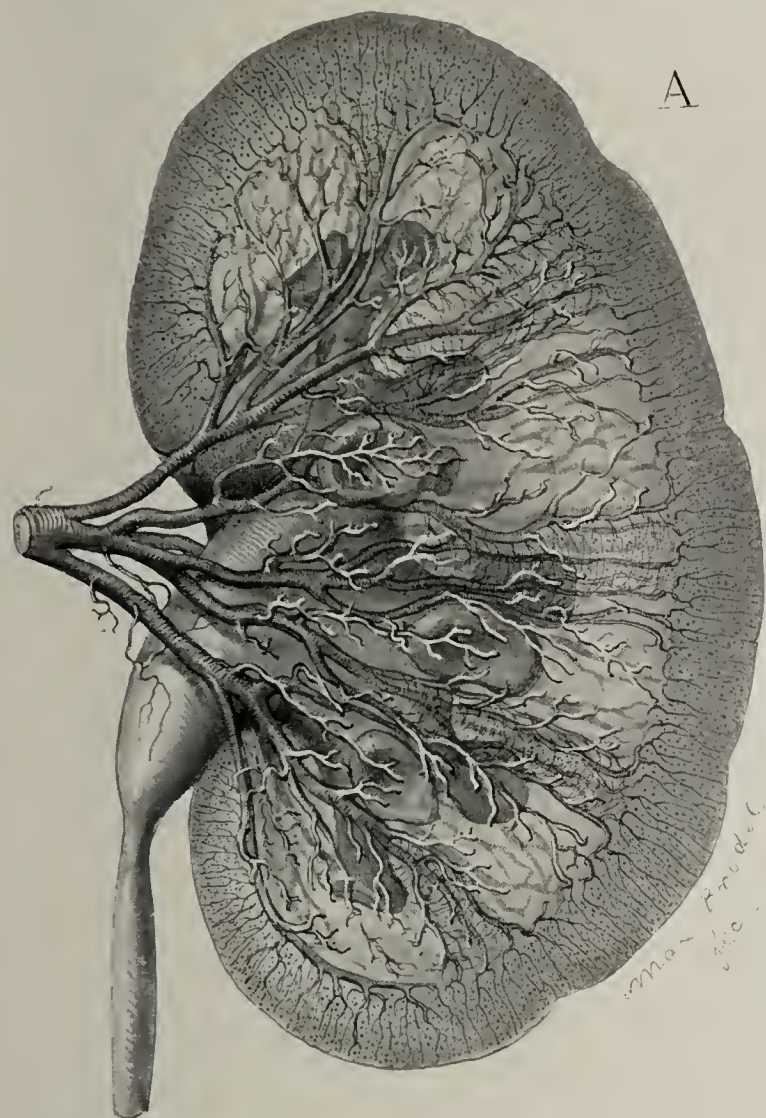
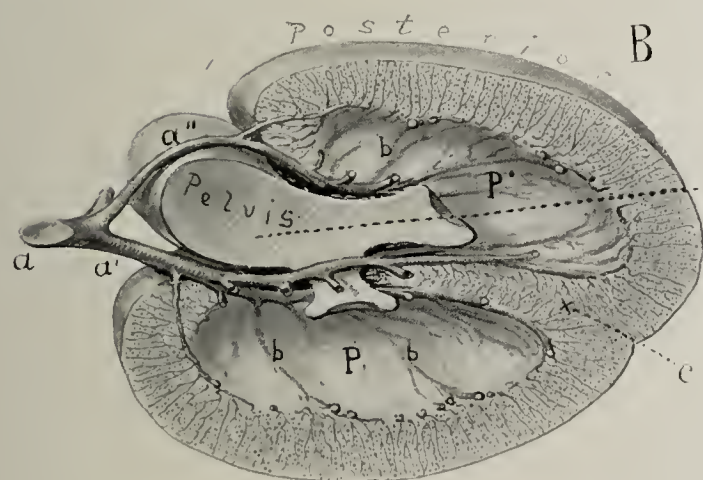


FIG. 3.—The renal artery and the distribution of its branches in relation to the pelvis.

A. Anterior view of a left kidney. There are 6 main branches seen entering the kidney substance. Only one of these (the third) passes posterior to the pelvis at the hilum, also small arteries coming from the upper and lower main branches are seen to pass posterior to the upper and lower calices. All the rest of the arteries pass anterior to the pelvis and its calices. The small branches to the cortex of the anterior portion of the kidney have not been drawn in order that the large branches and the pelvis might appear more distinctly.



B. Transverse section through the middle of the same kidney seen from above. The anterior branch of the artery supplies about $\frac{3}{4}$ of the kidney substance while the posterior branch supplies only $\frac{1}{4}$. The dotted line and arrow indicate the plane of arterial division.

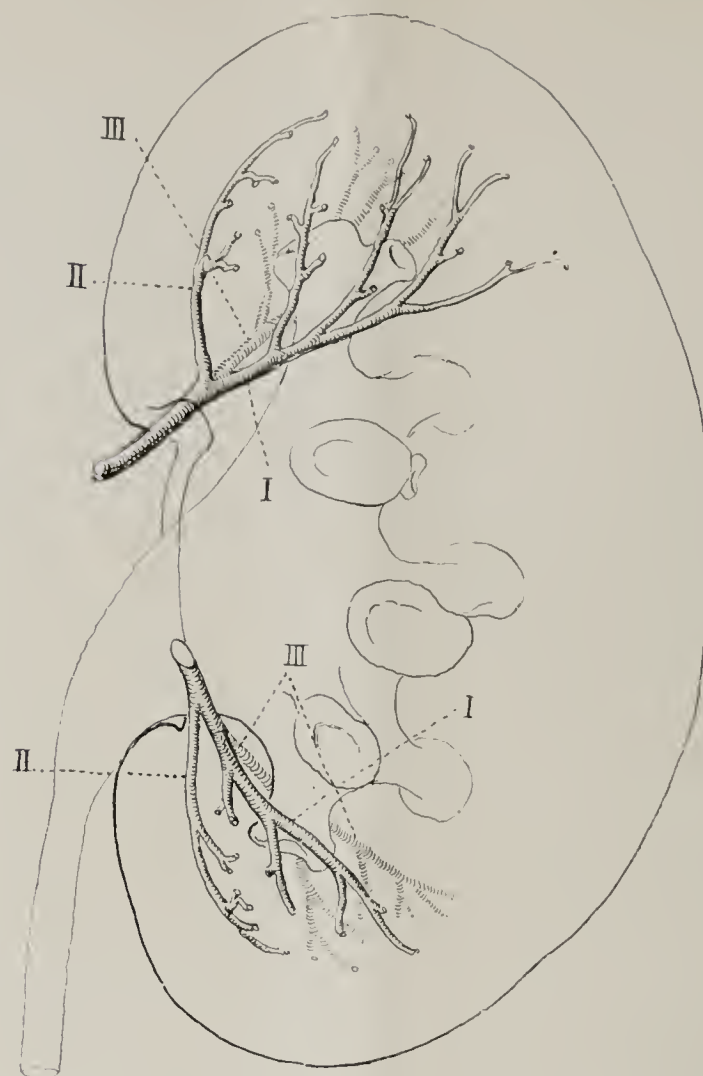


FIG. 4.—Arrangement of the arteries at the upper and lower pole. They come as single trunks from the main artery and run at an angle of 45° or more upward and downward to the vicinity of the major calices, where they divide into three branches.

I. Anterior branch.

II. Median branch.

III. Posterior branch.

The anterior and posterior branches are as a rule much larger than the median.

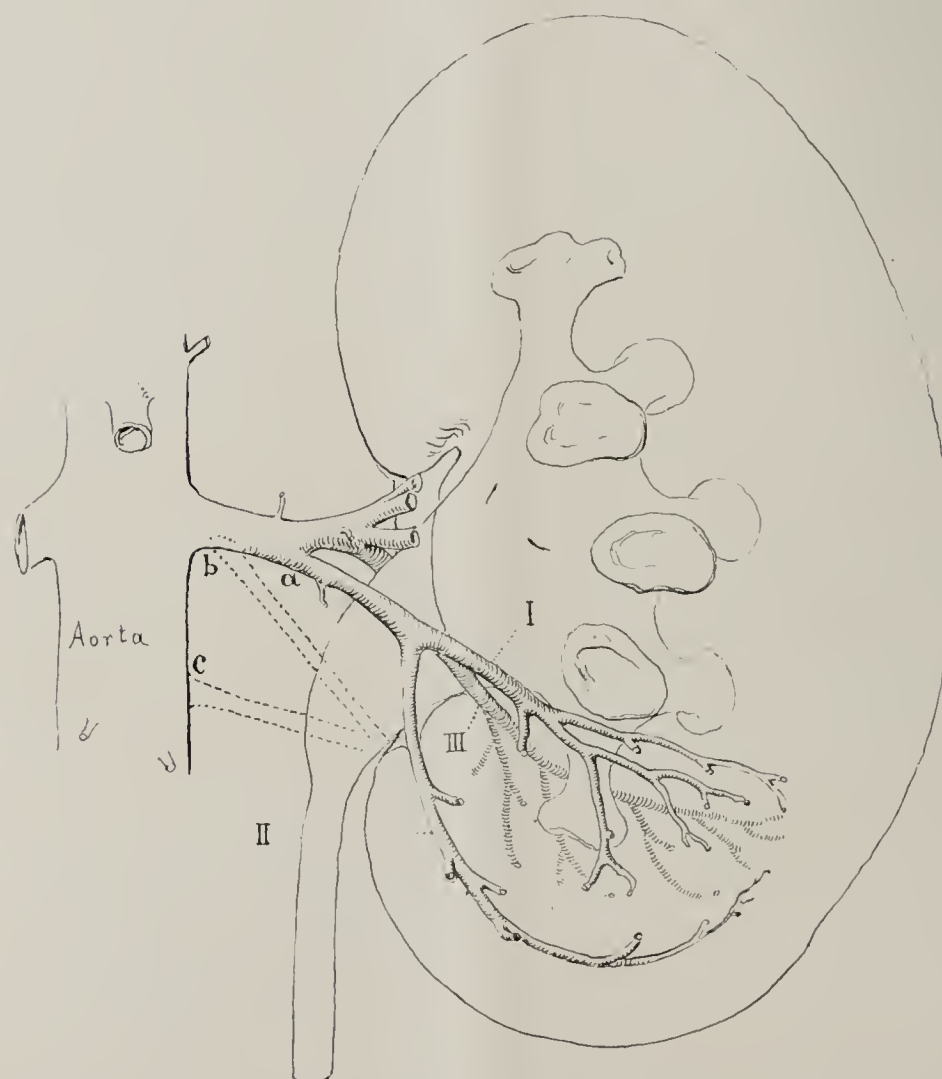


FIG. 5.—Variation of the median branch. This branch may be larger than usual and arise separately from the main artery at points *a* and *b*, or from the aorta direct (*c*). It may be as large as the renal artery itself, in which case it gives off branches I and III or more. Such an arrangement of the arteries is as a rule associated with an abnormal form and position of the renal pelvis.

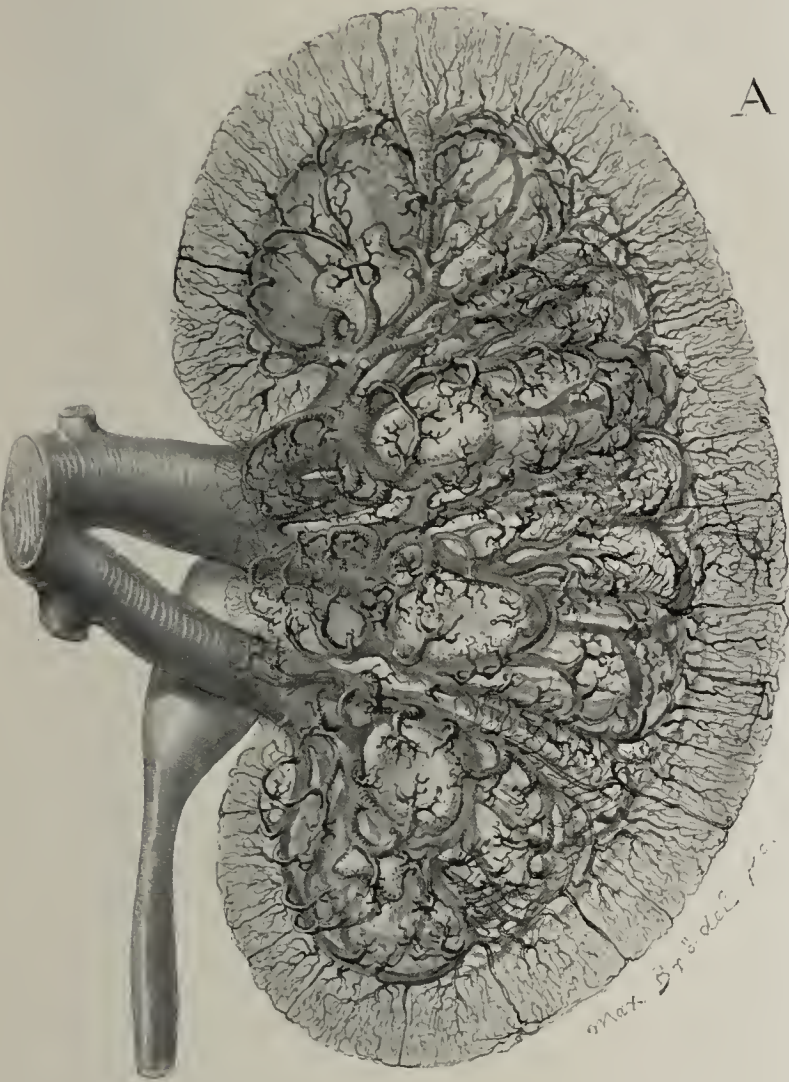
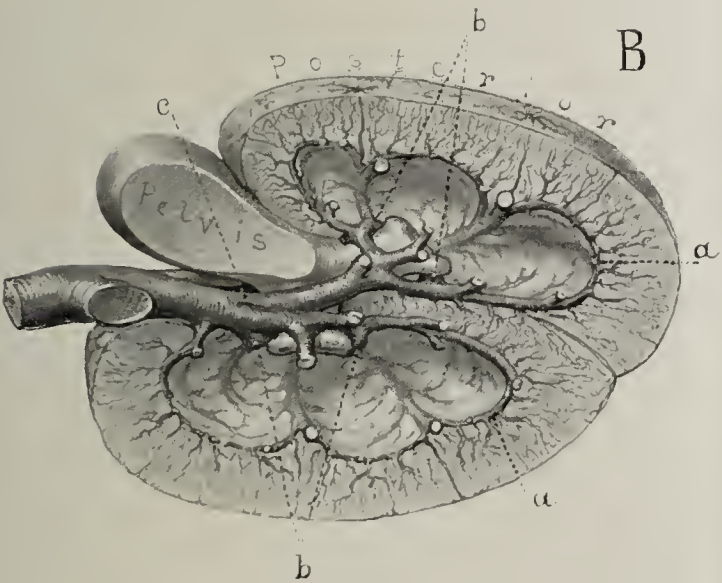


FIG. 6.—The renal vein and the relation of its branches to the pelvis of the kidney.

A. Anterior view of the left kidney. For the sake of clearness the small veins of the cortex of the anterior portion of the kidney have been omitted.



B. Transverse section seen from above. There is no collecting vein posterior to the pelvis; all the veins of the posterior region cross over to the anterior portion between the necks of the minor calices (*b*) to join the veins of the anterior region at a point indicated by *c*.



FIG. 7.—A normal left kidney.

A. Posterior view.

B. Anterior view.

C. Lateral view.

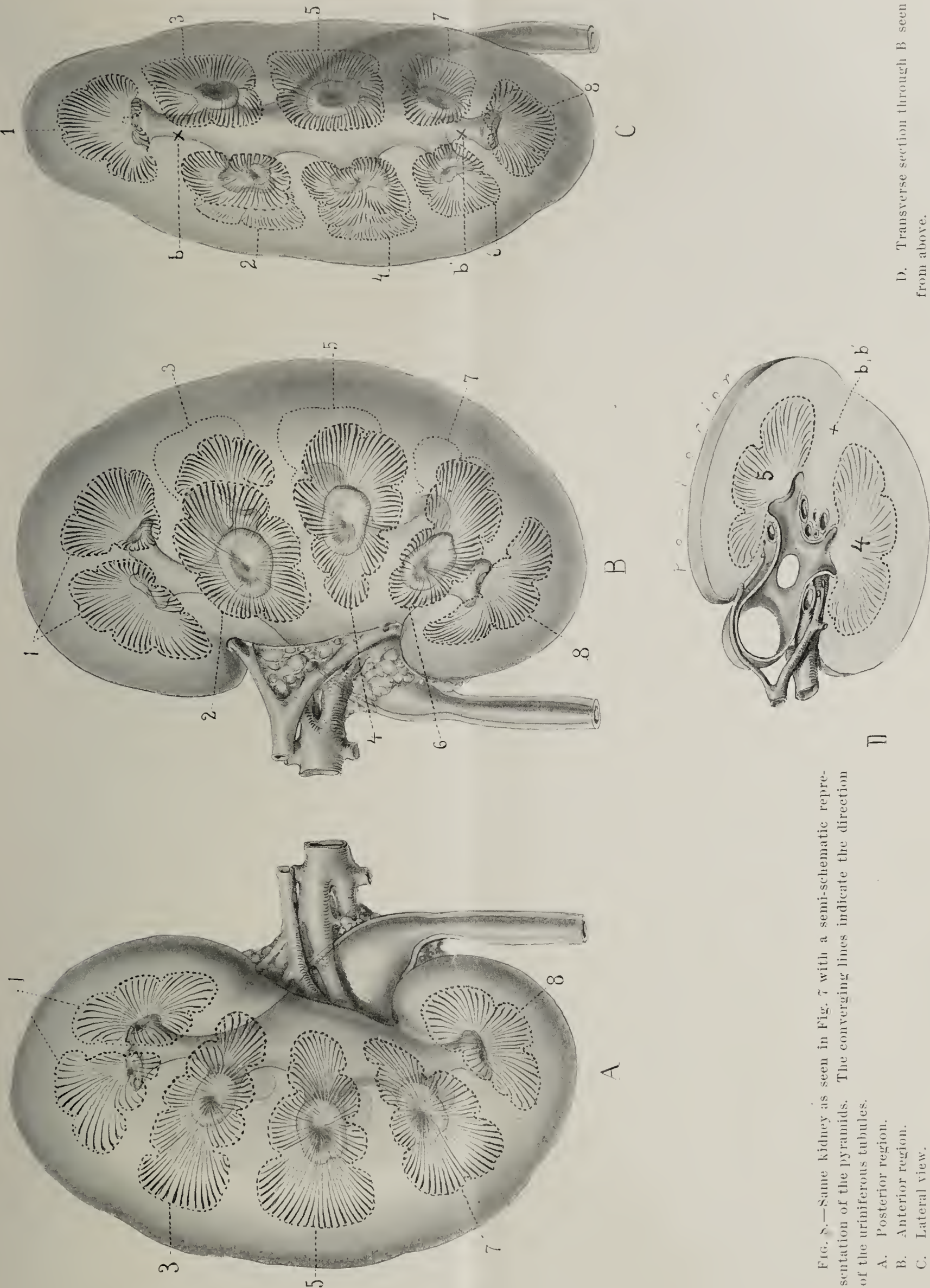


FIG. 8.—Same kidney as seen in Fig. 7 with a semi-schematic representation of the pyramids. The converging lines indicate the direction of the uriniferous tubules.

- A. Posterior region.
- B. Anterior region.
- C. Lateral view.

D. Transverse section through B seen from above.

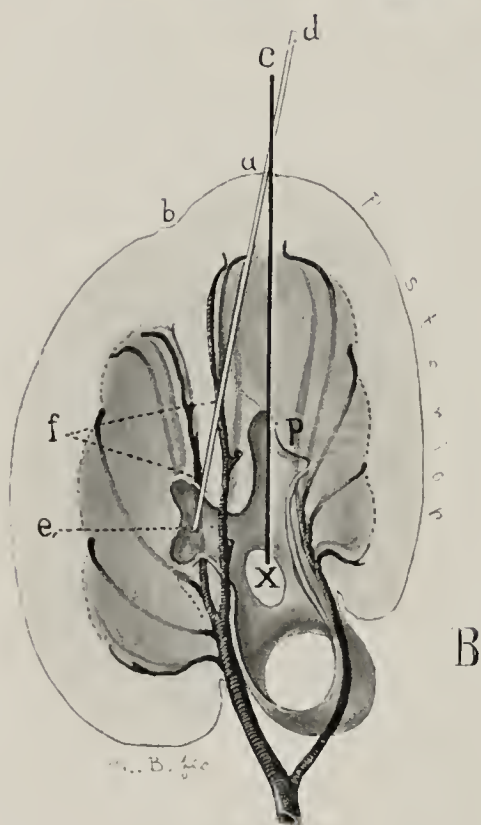
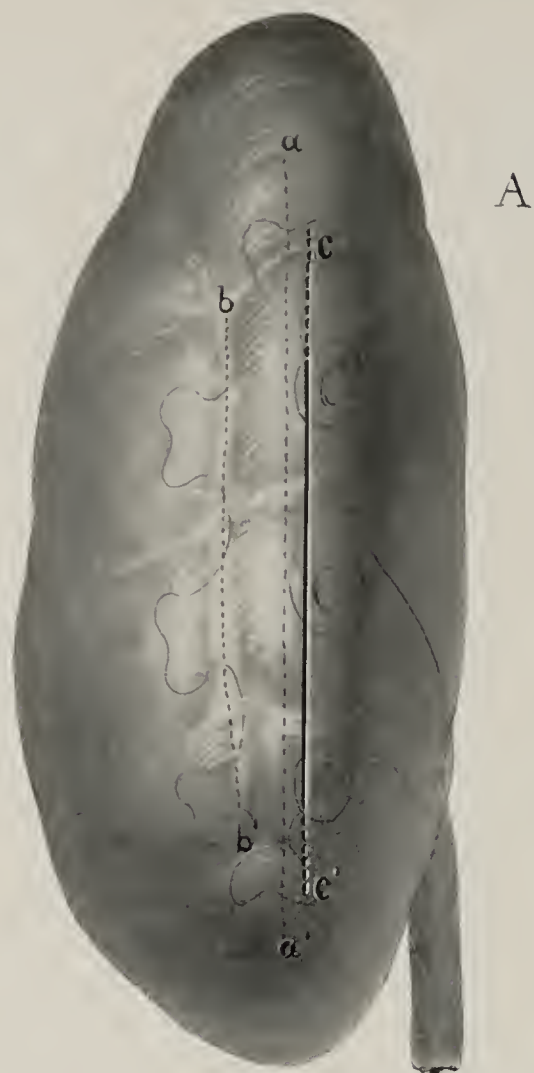


FIG. 9.—A. Lateral view of left kidney, showing the location of the most advantageous incision through the parenchyma in kidneys which have a normal arterial arrangement.

aa' Lateral convex border of kidney.

bb' Position of lateral column of cortical substance containing the vessels.

cc' Best incision.

B. *de* Incorrect direction of incision.

ce Correct direction of incision.

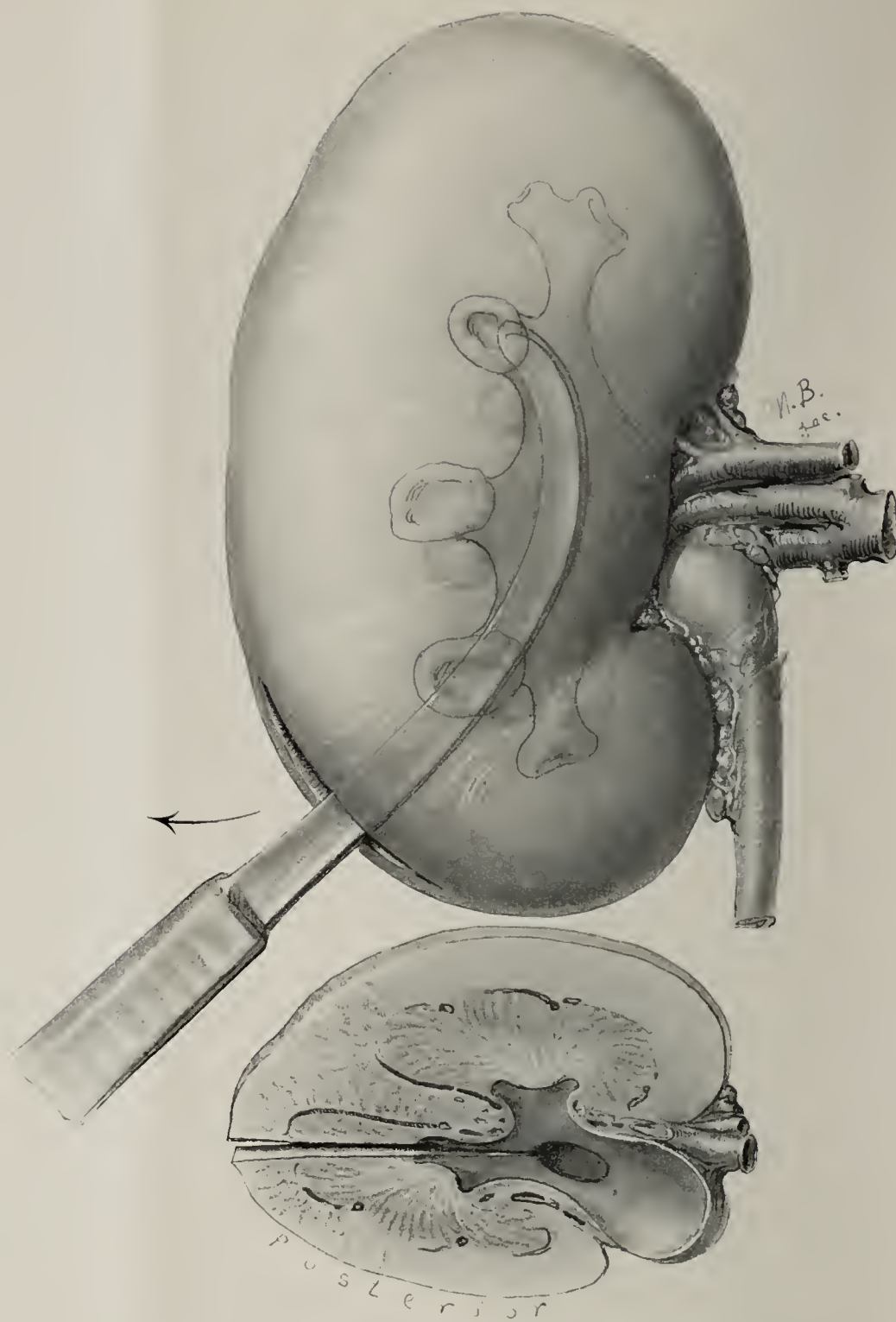


FIG. 10.—Posterior view of left kidney, showing method of exploring and opening the pelvis. The lower diagram indicates the direction of the incision in relation to the papillae of the posterior pyramids.

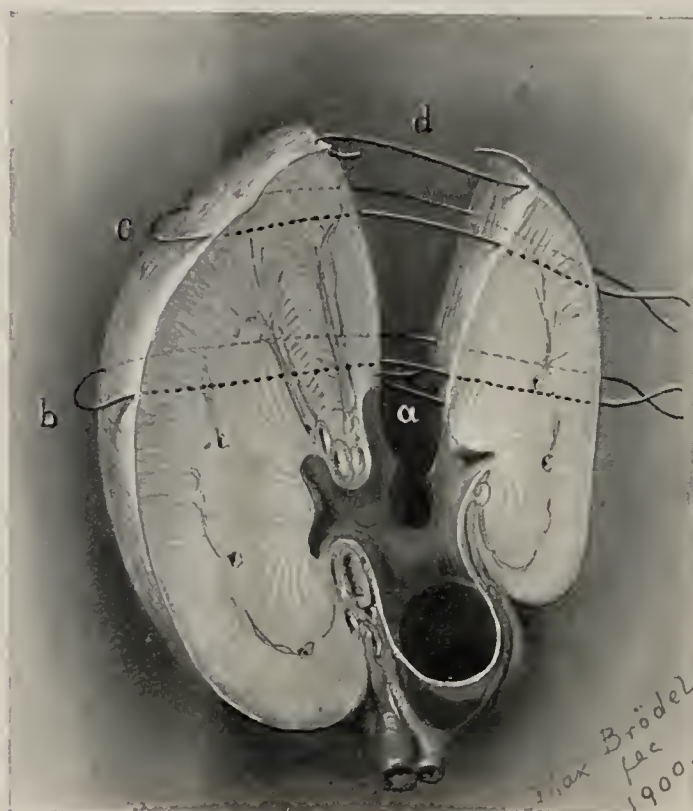


FIG. 11.—Imaginary transverse section through a kidney similar to Fig. 9 B, showing manner of placing the mattress sutures.

Max Brödel
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vessels of the kidney (three-fourths of the arteries and all of the veins) are found (see also Figs. 3 and 6).

As was said before, in lobulated kidneys this column is indicated as a distinct depression on the surface. The capsule seems thickened along this line and frequently forms a whitish band, to which the perirenal fat appears to be more intimately attached than elsewhere.

Lobulation of varying degrees of distinctness is found in the great majority of cases. The trained eye can detect this lobulation in kidneys which a novice would pronounce perfectly smooth. Should, however, the kidney present not the slightest depression or lobulation, the arrangement of the large stellate veins of the capsule will still serve to sufficiently locate the limits of the pyramids and the position of the important lateral longitudinal column (*b b'*, Figs. 7 and 8). These veins are found to be more conspicuous and are arranged in rows along the lines where the foetal lobulation has been. (See Fig. 7.)

The Incision and Subsequent Suture.—The above described landmarks should suffice to guide the surgeon in making his incision so that the kidney can be readily opened between its anterior and posterior arterial branches.

Fig. 9 A shows the lateral view of the kidney; *a a'* represents a line showing the lateral convex border; *b b'* indicates the position of the lateral longitudinal column bearing the large vessels; *c c'* is the line along which an incision should be made. Diagram B shows the direction in which the knife should pass. An incision through the middle of the kidney (*d e*), would be inadvisable, inasmuch as it would cut through large vessels in region *f* and would fail to open the posterior calices. The proper direction is indicated by *c x*, the knife remaining in the posterior half of the kidney. The cut should be made anteriorly to the posterior papillæ (*p*) in order to avoid severing the collecting tubules of the posterior pyramids. It is advisable to palpate if possible the vessels and the pelvis at the hilum before making the incision, and if their arrangement is found to be normal, *i. e.* the pelvis at the posterior region of the hilum and the great majority of vessels anterior to the pelvis, then the above described procedure is applicable.

I wish to add a few suggestions as to the incision itself and also as to the subsequent suture.

A short incision is made into the lowermost posterior calyx if possible by means of blunt dissection (Fig. 1 A 7), and through this incision the pelvis is explored. In a collapsed state of the renal pelvis it may be difficult to enter one calyx. In such cases a moderate distention of the pelvis with sterile water or boric solution will facilitate the procedure considerably. If this short incision does not prove satisfactory, the three calices (3, 5, 7) should be carefully opened by means of an incision from within to the surface (Fig. 10). A curved knife will best answer this purpose. A glance at Fig. 3 A shows that short transverse incisions through the anterior or posterior parenchyma may produce little hemorrhage, provided they do not come too near the hilum. However, such incisions never open the pelvis satisfactorily.

The arrangement of the vessels in the kidney suggests the mattress suture as best adapted for approximating the two cut surfaces. Simple interrupted sutures almost always tear the tissues and produce an insufficient union. The mattress sutures are placed at right angles, or nearly so, to the large vessels and thus effectively prevent any tearing of the kidney substance. If the bight of the suture be $1\frac{1}{2}$ to 2 cm., no strangulation of kidney substance should result. The sutures should be applied in the manner represented in Fig. 11.

I. The pelvis is approximated with fine catgut sutures (*a*). These ought to be placed between the calices and take in only the fat, the outer fibrous coat and the muscular layers. The mucous membrane should not be included.

II. The second system of sutures should also be of catgut and should unite the region of the papillæ. They should be mattress sutures (Fig. 11 *b*) and are best placed by means of a long straight three-cornered needle with a blunt point, so that no injury to the large vessels results. A possible oozing would only serve to tighten the grip of these sutures and thus render them more effective.

III. The third system of catgut sutures should also be mattress sutures and be placed parallel to the second through the cortex near the bases of the pyramids (Fig. 11 *c*). Occasionally the third system of sutures is superfluous.

IV. The capsule is then closed in the usual manner (Fig. 11 *d*).

NOTES ON AËROBIC SPORE-BEARING BACILLI.

BY W. W. FORD, M. D., D. P. H.,

Fellow in Pathology, McGill University, Montreal.

(From the Molson Pathological Laboratory.)

The presence of spore-bearing bacilli in the contents of the intestinal tract—in the normal organs and in various serous exudates—is of fairly frequent occurrence in routine bacteriological investigation, but the identification of such micro-organisms does not always present that ease which is requisite for the convenience of the routine worker.

Aside from the well-known forms of *Bacillus subtilis* and *Bacillus mesentericus*, other varieties of spore-bearing bacilli are recognized with difficulty, owing to the inadequate descriptions usually found in text-books devoted to bacteriology, where the pathogenic bacteria naturally receive the greatest attention.

During the past year a number of such forms have been isolated and studied in the Molson Pathological Laboratory and an attempt has been made to group these forms together, using as a basis of classification the table of constant characters recently adopted by Fuller and Johnson.

The various reactions of these bacilli on the usual culture media have been estimated in so far as possible with reference to the possession, or lack of possession, of any of these constant characters, and the results of this study are embodied in the chart which accompanies this paper. Some varieties here described may be identical with bacilli already referred to in the literature, but an attempt to recognize them positively has not met with success, and on this account they have been looked upon as either new species or new varieties of old species.

While such a description as this may at first seem inadequate, experience has shown that morphology alone fails to reveal the identity of our ordinary micro-organisms and that such a chart, as the one here utilized for bacteriological protocols, is of the greatest assistance in species differentiation.

These spore-bearing bacilli were isolated at various times in the laboratory under the ordinary conditions of aerobic cultivation and are purely aerobic or facultative anaerobes in character. They may be divided into two groups—pathogenic and non-pathogenic—in each group being included here five different varieties. The criterion of pathogenicity is in all cases determined by the intraperitoneal inoculation of a mouse with a 1 cc. dose of a 24-hour old culture of the bacillus in question.

The members of both groups grow with ease on the routine culture media, the production of spores taking place rapidly under the usual conditions, a greater abundance of spores naturally being observed on the older cultivations. These bacilli possess certain characters in common: The carbohydrates are never fermented with the production of gas; milk is coagulated, probably by the action of enzymes, as the reaction remains neutral or alkaline until after the digestion of the casein when a small amount of acid is produced. The liquefying powers of these bacilli are especially well marked, often casein, gelatin and blood serum alike being affected.

While the correlation of different biological properties in bacteriology has as yet met with rather indifferent success, yet it is a significant fact that marked liquefying powers are often associated with the capacity of spore-formation. Similar deductions cannot be drawn with regard to motility, which occurs, one might say, almost at random and cannot be associated with other characters, as for example, pathogenicity.

The growth on potato is usually very abundant, this growth serving at times as a diagnostic feature. The present status of our knowledge of the conditions under which indol and a faecal odor are produced, does not permit any reliable data to be drawn from these reactions, but their importance, when given, renders their careful study necessary.

Under *Group 1*, pathogenic spore-bearing bacilli, have been included five different varieties:

Bacillus A is a capsulated bacillus which bears some re-

semblance to *Bacillus mucosæ capsulatus*, but differs in so many reactions, especially in its capacity to form spores, that it has been placed in this group. It was isolated from the liver of a healthy rabbit. Its morphology is that of long rods with square-cut ends in fresh cultures, the bacillus appearing singly or in short chains. In old cultures it loses its characteristic form, appearing as chains of short oval bacilli with the phenomenon of polar staining especially well marked, two small refractile granules being seen at either end of each individual. The capsule is apparent with all dyes, but it is most readily observed when the bacillus is found in the tissues of an inoculated animal when the organism itself appears in its original character as a long straight bacillus staining deeply and regularly throughout.

Bacillus A is non-motile, forms a characteristic scum on fluid media, liquefies gelatine, coagulates milk without acidifying or digesting the casein. It is pathogenic to mice, guinea-pigs and rabbits, all of which died in from 24 hours to 10 days, revealing at autopsy no special appearances beyond those seen in infections in general and furnishing pure cultures of the bacillus from the internal organs.

Old cultures of this bacillus—from which, by the way, a peculiar sickening odor is obtained—will kill even as large animals as rabbits in two hours, the animals dying with all the symptoms of profound toxæmia.

Bacillus B was obtained from the kidney of a healthy rabbit and in its morphology is not unlike the preceding variety. It is a long bacillus with square-cut ends—without a capsule—in old cultures growing out into degenerate forms, showing the greatest diversity in morphology. Spore-formation occurs with great rapidity.

Bacillus B is non-motile and does not form a scum on broth, liquefies gelatin, coagulates milk, digesting the casein and producing an acid reaction. It is pathogenic to mice and guinea-pigs, which survive from 24 to 72 hours, but is not pathogenic to rabbits.

Bacillus C was obtained from the same kidney which furnished the cultures of *Bacillus B*. It is a long, narrow bacillus with rounded ends, quite regular in shape and maintaining its regularity even in old cultures. Its growth is somewhat slower than most of the spore-bearing forms.

It is actively motile in 24-hour old cultures, forms a pellicle on broth, liquefies gelatin and blood serum, coagulates milk and digests the casein with the production of an acid reaction. It is pathogenic to mice, guinea-pigs and rabbits, the animals succumbing in from one to three days, and showing the presence of the bacillus in large numbers in all of the internal organs.

Bacillus D was obtained from a rabbit's kidney. It is a long, thick bacillus growing at times in short chains; it exhibits polar staining to a marked extent, peculiar unstained areas often being visible in the bodies of the bacilli.

It is actively motile, liquefies gelatin, casein and blood serum, but does not produce acid or coagulate milk. It is pathogenic to mice and guinea-pigs, these animals dying after a lapse of from 12 to 15 days, the characteristic organism being then obtained from the different organs.

Bacillus E is a large bacillus obtained by Dr. Yates from a pleural exudate, which in its morphology cannot be positively distinguished from the preceding forms. Its varied reactions on culture media testify to its originality. It grows as a pellicle of broth, liquefies gelatin but not blood serum, and coagulates milk, digesting the casein. Mice are killed by intraperitoneal inoculation in from 3 to 4 days.

Prototypes of spore-bearing bacilli which are non-pathogenic are *Bacillus mesentericus* and *Bacillus subtilis*—bacilli which are probably the most common forms of laboratory contamination. For completeness in the chart the reactions of these bacilli have been either estimated or adopted from Fuller and Johnson. With these, however, may be grouped three other bacilli:

Bacillus F was obtained from the liver of a guinea-pig. It is a thick, plump bacillus, at times in short chains, regular and deeply staining. In its morphology it is somewhat similar to *mesentericus* but is rather smaller than the potato bacillus, from which it differs, moreover, in not forming a wrinkled growth on agar nor a pellicle on broth, and in not growing in the closed arm of the fermentation-tube nor producing a faecal odor.

Bacillus G, isolated from the stomach contents of an autopsy subject, is evidently a variety of *Bacillus mesentericus* which it closely resembles in morphology but is distinguished by liquefying only gelatin and casein, not blood serum, and by its failure to give a characteristic growth on potato.

The last member of this group, *Bacillus H*, was obtained by Dr. Nicholls from the liver of a healthy cat. It is the only one of this group which is non-motile and is distinguished from the other members by not forming a scum on broth, in not causing a wrinkled growth on agar and in not growing in the closed arm of the fermentation-tube. It liquefies gelatin and blood serum, coagulates milk, digesting the casein and producing an acid reaction.

It is hoped that this plan of description of bacteria may prove of value to observers in different laboratories, and should its adoption be brought about in different universities, a considerable advance can be made in settling the complex problems of species differentiation.

NOTE:—Several of the bacteria here described are said to be facultative anaërobes in character but without the capacity of growing in the closed arm of the fermentation-tube. The latter reaction has been utilized as a criterion of anaërobic growth by a number of observers, it being maintained that the growth of the organism will exhaust the oxygen from the open bulb leaving an oxygen free medium in the closed arm, in which the facultative anaërobes will always grow. This apparent contradiction in reaction is difficult of explanation unless one considers that certain bacilli, aërobic and facultative anaërobes in character, grow with greater avidity in a medium which has free access to oxygen, thus being attracted to the open bulb of the fermentation-tube, where they grow luxuriantly, yet nevertheless being capable of development in an atmosphere devoid of this substance, as is proved by cultivation in conditions suitable for anaërobic growth. Compare in this connection the chart of Fuller and Johnson where the *Bacillus annulatus* of Wright is described as a facultative anaërobe and yet failing to grow in the closed arm of the fermentation tube.

TYPE.	NAME.	SOURCE.	MOR- PHOLOGY.		BIOLOGY.																		PATHO- GENICITY.		
					CULTURAL FEATURES.								BIOCHEMICAL FEATURES.										MICE.		
Bacillus.	Diameter greater than one mikron.	Motile.	Spores.	Broth.	Agar.	Gelatin Plate.	Potato.	Fermenta- tion Tube.	Grows at body temp.	Facultative anaërobo.	Affected by range of reaction.	Lique- faction.	Gas produce- tion.	Nitrites produced.	Indol.	Faecal odor.	Milk.	Agar.	Intraperitoneal inoculation.						
Scum.	Turbidity.	Dull.	Wrinkled.	Characteristic appearance.	Visible.	Luxuriant.	Growth in closed arm.					Gelatin.	Casein.	Blood serum.	Dextrose.	Saccharose.	Lactose.	Acidity before coagulation.	Coagulation.	Acidity after coagulation.	Chromogenesis.	Fluorescence.	Most favorable reaction.		
Spore-bearing Pathogenic Bacilli.	Bacillus A.	Liver of rabbit	+	+	-	+	+	+	+	+	+	+	+	+	+	-	-	-	-	+	+	-	-	+	+
	Bacillus B.	Kidney of rabbit	+	-	-	+	-	+	+	-	+	+	+	+	-	-	-	-	+	+	+	-	-	0	+
	Bacillus C.	Kidney of rabbit	+	+	+	+	+	+	-	-	+	+	+	+	-	-	-	-	+	+	+	-	-	0	+
	Bacillus D.	Kidney of rabbit	+	-	+	+	+	+	-	-	+	+	+	+	-	-	-	-	+	+	-	-	-	0	+
	Bacillus E.	Pleural exudate	+	+	-	+	+	+	-	-	+	+	+	-	-	-	-	-	+	+	-	-	-	+	+
Spore-bearing Non-pathogenic Bacilli.	B. Subtilis.	?	+	+	+	+	+	-	+	+	+	+	+	+	-	-	-	-	?	+	?	-	-	?	-
	B. Mesentericus.	?	+	+	+	+	+	+	+	+	+	+	+	+	-	-	-	+	-	+	-	-	+	-	
	Bacillus F.	Liver of guinea-pig	+	-	+	+	+	+	-	-	+	+	+	+	-	-	-	+	+	-	+	-	0	-	
	Bacillus G.	Stomach of man	+	+	+	+	+	+	+	+	+	+	+	-	-	-	+	+	-	+	-	-	0	-	
	Bacillus H.	Liver of cat	+	+	-	+	-	+	+	-	+	+	+	+	-	-	-	-	+	+	+	-	-	+	-

NOTE.—The media here employed were prepared according to the directions given in the 1897 report of the Committee of American Bacteriologists with the exception that the reactions have been rendered neutral to phenol-phthalein. The plus and minus signs have also been used in the manner directed by this Committee.

SUMMARIES OR TITLES OF PAPERS BY MEMBERS OF THE HOSPITAL AND MEDICAL SCHOOL STAFF APPEARING ELSEWHERE THAN IN THE BULLETIN.

SIMON FLEXNER, M. D. Nature and Distribution of the New Tissue in Cirrhosis of the Liver.—*University Medical Magazine*, November, 1900.

ANDREW H. WHITRIDGE, M. D. Report of a Case of Tetanus with Recovery.—*Philadelphia Medical Journal*, October 20, 1900.

WILLIAM W. FORD, M. D. Venous Thrombosis in Heart Disease.—*Philadelphia Medical Journal*, November 17, 1900.

WILLIAM SYDNEY THAYER, M. D. Observations on the Blood in Typhoid Fever.—*Journal of the Boston Society of Medical Sciences*, Vol. 5, No. 1, 1900.

ROBERT L. RANDOLPH, M. D. Ossification of the Choroid Leads to the Identification of the Body in an Insurance Case.—*Journal of the American Medical Association*, November 10, 1900.

HUNTER ROBB, M. D. Remarks upon the Post-Operative Treatment; with Especial Reference to the Drugs Employed in 114 Consecutive, Unselected Abdominal Sections without a Death.—*Cleveland Medical Gazette*, October, 1900.

ADELAIDE DUTCHER. Where the Danger Lies in Tuberculosis.—*Philadelphia Medical Journal*, December 1, 1900.

WILLIAM OSLER, M. D. On the Study of Tuberculosis.—*Philadelphia Medical Journal*, December 1, 1900.

J. HALL PLEASANTS, M. D. A Case of Acromegaly in a Negro Associated with a Low Grade of Giantism.—*Maryland Medical Journal*, December, 1900.

ANDREW H. WHITRIDGE, M. D. The Importance of Instruction in Medical Schools upon the Modification of Milk for Prescription Feeding.—*Maryland Medical Journal*, December, 1900.

THOMAS R. BROWN, M. D. A Review of Some of the Recent Work on the Physiology and Pathology of the Blood.—*Maryland Medical Journal*, December, 1900.

J. H. MASON KNOX, PH. D., M. D. Compression of the Ureters by Myomata Uteri.—*The American Journal of Obstetrics*, September and October, 1900.

Twenty-five cases are collected from the literature and the gynecological records of the Johns Hopkins Hospital in which myomata uteri were found to have exerted more or less pressure upon one or both ureters. The small number of such cases reported is probably due to the fact that moderate grades of ureteral compression from this cause produce few definite symptoms and the condition is consequently overlooked.

The cases are gathered in several groups according to the severity of the ureteral and renal involvement; thus:

Group A.—Moderate ureteral involvement, 8 cases.

Group B.—Pronounced ureteral pressure, 5 cases.

Group C.—Mechanical destruction of renal substance, 1 case.

Group D.—Ureteral pressure with inflammation, associated with

a. Chronic nephritis, 2 cases.

b. Congenital cystic kidneys, 1 case.

c. Pyogenic infection, 2 cases.

d. Pyogenic infection, severe, 3 cases.

e. Kidney, a pus sac, 3 cases.

The several important features suggested by analysis of the cases are then discussed. It is found that this ureteral complication during the growth of a myomatous uterus occurs usually at middle life, that the tumor mass is usually large in size and firm in consistency, and that although the pressure upon the ureter can be exerted at any point or along much of its course, the most frequent seat for compression is at the pelvic brim. Of the complications the formation of adhesions which often render operative interference difficult and the secondary infection of the urinary tract are most important. The pathology of the condition is briefly referred to, beginning with simple dilatation of the ureters and renal pelvis and progressing, unless relieved, to extreme grades of hydronephrosis and hydronephrosis, or if the element of infection is added to, pyoureter and pyelonephrosis. There are but few definite signs or symptoms of the condition other than a partial retention of the urine in advanced cases. Hence the diagnosis must be made by a careful direct examination bimanually and with the cystoscope through which the ureters can be catheterized when their involvement is suspected.

Three lines of treatment are suggested: (a) expectant, applicable when the ureteral symptoms are slight and give no discomfort to the patient; (b) palliative, permissible only when the ureteral compression is moderate and is not becoming worse or when the condition of the patient is so alarming as not to tolerate a more radical method; (c) radical, that is, the removal of the compressing mass. This should be undertaken unless contraindicated whenever there is definite indication that the ureters are markedly compressed. The following conclusions are drawn:

1. That some compression of the ureter is produced by a large proportion of all large myomatous uteri.

2. The resulting hydronephrosis and hydronephrosis may continue for years and give rise to no discomfort to the patient.

3. The presence of a dilatation of the ureter and renal pelvis however slight, lowers the resistance of these organs to toxic and infectious agents, and hence inflammatory conditions of the ureters and kidneys not infrequently follow ureteral compression.

4. This being the case in all instances of uterine myomata, the possibility of ureteral involvement must be considered. When such a condition is suspected every effort should be made by means of direct examination, by ureteral catheter, etc., to arrive at an accurate diagnosis.

5. Exploratory incision is occasionally justified to establish a diagnosis.

6. The ureters should be inspected whenever the abdomen is opened for the removal of the tumor.

7. A myomatous mass found to be exerting undue pressure upon one or both ureters should be removed, if possible, unless operative interference is contraindicated.

8. Such serious sequelæ of ureteral compression as extreme hydronephrosis, pyelonephrosis, etc., should receive appropriate treatment.

The references to the cases and a table are appended.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

October 15, 1900.

The meeting was called to order by the retiring president, Dr. Henry M. Thomas.

Dr. Thayer presented resolutions expressing the feelings of the Society at the death of Dr. Lazear, which were unanimously adopted.

The annual election of officers was held and Dr. William H. Welch was elected president, and Dr. G. Brown Miller secretary, for the coming year.

Case of Asthma with Cyanosis, Extensive Purpura, Painful Muscles, and Eosinophilia. DR. OSLER.

This is an unusual case in several respects. This young man came in on the 3d of October complaining of pain in the abdomen. His personal and family history are negative so far as this present condition is concerned. He had eaten abundantly of pork, and it is not known whether it was raw or cooked, as he is a Pole and it is difficult to understand him.

His present illness began with a chill, accompanied by pain in the abdomen and on the three following days he had nausea and vomiting. There was no diarrhoea. There had been cough and expectoration since the onset of the illness and he had been confined to bed. On the night of admission the most remarkable feature noticed was a very deep cyanosis. The respiration was somewhat labored, being about 30 to the minute, but there was no urgent dyspnoea. There were numerous dry râles and much wheezing in the tubes. He remained in this condition of remarkable cyanosis with practically no fever, except a slight one on the third day; indeed, as a rule, his temperature has been subnormal. The cyanosis was extreme and with it, which is noteworthy, he remained constantly recumbent.

On October 7, in addition to the cyanosis, petechiae appeared over the body, first on the face and chest and then over the skin of the entire body except the legs. He presented a unique appearance, so far as our experience here is concerned, and looked very much like a case of malignant hemorrhagic smallpox. A differential count showed 11 per cent of eosinophiles. On the 8th of October he showed great tenderness of the muscles. The slightest touch on the muscles of the arms or legs caused him to wince. A portion of muscle was excised and showed marked degeneration with a great deal of fat in the fibres, but no trichinae. On the 9th his leucocytosis rose to 52,000, the petechiae had increased, his face was swollen, and he looked to be in a very critical condition. He was, however, rational, apparently comfortable and took his food fairly well. On the 11th the eosinophiles had risen to 25 per cent. Yesterday the cyanosis began to disappear. Cultures from the blood are negative and there is no Widal reaction. There is a trace of albumin and few granular casts.

Of the groups of cases of cyanosis there is one in which the air cannot get to the blood—the respiratory group; a second group in which the blood cannot get to the air—the cardiac; and there is a third group in which there are changes in the hemoglobin, such as cases of poisoning by carbon monoxide or the coal-tar products. There are three conditions in which, in hospital practice, we see extreme cyanosis with comparative comfort: First, the cases of chronic emphysema and asthma. A patient will come in completely cyanosed, quite livid, and yet fairly comfortable and not especially short of breath. Secondly, the cases of congenital heart disease. Thirdly, the cases of antifebrin and antitoxin intoxication.

In this case there has been no methemoglobin in the blood, and I think it cannot be regarded as belonging to the toxic form. He has had some asthma and emphysema; with that would agree the condition of eosinophilia. The question is whether or not he has had a myositis and possibly trichinosis. That cannot be determined until we have further examined the muscle. (It is negative, too).

DISCUSSION.

DR. WELCH.—Are there any abnormal leucocytes, such as are not normally found in the blood?

DR. FUTCHER.—No. There are many cells, however, which it is difficult to classify, because it is hard to say whether they are eosinophiles or polynuclears; they seem to stay in an intermediate stage.

DR. WELCH.—Dr. Osler spoke of the similar appearance to black smallpox when the petechiae were so abundant. It has been claimed that the leucocytic count is quite characteristic in smallpox; in fact, so definite in its proportions as to be a decided help in diagnosis.

Bisection of the Uterus in Hysterectomy. DR. KELLY.

[See BULLETIN for January, 1901.]

Exhibition of Surgical Cases. DR. MITCHELL.

Four cases of typhoid perforation were described, and one of appendicitis. (To appear in full in a later number.)

DISCUSSION.

DR. OSLER.—This last case is exceedingly interesting, for it is, if I remember rightly, the only case of abscess of the liver in connection with typhoid that we have had in the hospital. I have seen two such cases but it is one of the rarest of all complications of the disease. The positive Widal, the hemorrhages, the absence of ameba and the history make it quite clear as to the character of the original disease.

DR. THAYER.—I wish to ask, referring to the case in which the appendix was removed, how long before death the last rise of leucocytes was observed; whether it was, as the Germans say, due to the death agony or to something else.

DR. MITCHELL.—It was several hours before death.

Dr. Keen in his remarks upon surgical complications speaks of 21 cases of liver abscess with two recoveries.

DR. WELCH.—I remember seeing one case of a somewhat different type, which occurred before the days of making cultures, in which there were thrombosis of the intestinal mesenteric veins and multiple metastatic abscesses throughout the liver instead of one large abscess.

DR. OSLER.—I think there is one point that ought to be quite clear in reference to the condition of the peritoneal surfaces of typhoid ulcers. Such a condition as that described by Dr. Mitchell does not indicate that perforation has of necessity occurred in those ulcers. Every deep ulcer is sure to have a great deal of injection about it, or even lymph on it, and sometimes in very intense and severe cases that come to autopsy at the end of the second week you can count through the serosa every Peyer's patch that is involved. I do not think, therefore, that it would be right to say, even with the most intense swelling and redness, that it necessarily follows such an ulcer will perforate.

Report of Cases from the Garrett Hospital for Children. DR. W. B. PLATT.

a) Bow-Leg, b) Knock-Knee, c) Epispadias. Patients shown in each case with photograph of condition previous to operation.

The cases of bow-leg and knock-knee are presented together to illustrate the opposite conditions. We know that infants at birth, and also long before they have borne pressure upon the limbs at a later date, present bow-legs. These, as well as the bow-legs acquired after walking, often become straight spontaneously. What chiefly interests us is, what to do if this spontaneous straightening does not occur. If spontaneous correction does not take place before the age of four years, or if orthopedic appliances properly applied do not accomplish the purpose before that age, there is little reason to hope for further improvement without operation, on account of the hardening of the bones that quickly ensues in such cases.

In bow-leg we have to deal with a general curvature of the femur, tibia, and fibula, which is accentuated at certain points. This curvature is always more or less outward, and often forward as well.

The extreme curvature is doubtless due chiefly to the weight of the body upon softened bones, and in but slight degree to muscular tension.

Rickets is clearly the cause of the softening in the greatest portion of cases. If knock-knee (like bow-legs) be due to rickets we would expect an inward curve instead of the angle which we find. Here we have a disproportionate growth of the inner portion of the lower end of the femur, sometimes also of the upper end of the corresponding part of the tibia. A practical point is, that in extreme bow-leg we find flat foot, whereas in extreme knock-knee we frequently get an acquired club foot.

The gait in the two classes of cases is exactly the reverse,

the one of the other. The two patients here shown are each five years of age. The "bow-leg" is somewhat deficient mentally. The deformity in the latter case was remedied by dividing the tibia nearly through, near the middle, with a chisel, proceeding from the anterior and inner aspect, outward. The bone was then fractured at this point, and the leg straightened. The fibula fractures with the tibia. The entire limb was now put up in plaster for three weeks. The usual result is an entire success. After both knock-knee and bow-leg osteotomies, there is a good deal of oozing, and the plaster bandage is not infrequently stained through. If the operation has been performed aseptically, there is never any trouble.

Osteotomy for knock-knee is performed on a different plan and in a different place. Mackewen's place of election is three-quarters of an inch above the adductor tubercle on the inner aspect of the femur. The chisel is driven about two-thirds of the way through the femur, going upward and downward after entering the chisel, so as to divide the anterior and posterior aspects of the bone. After withdrawing the chisel the limb is forcibly straightened. This impacts the lower fragment into the upper, and chiefly on the innermost line of the division. The undivided part of the bone bends like a hinge without fracture. The limb is immediately put up in plaster in a slightly over-corrected position.

In both the above cases, I operated upon the right limbs, while Dr. Cone operated upon the left knock-knee, and Dr. Ratcliffe upon the left bow-leg.

c) Epispadias. The patient, W. L., is twelve years of age. He has been operated upon six times during the past seven years. Five operations are theoretically called for, but one or more of them usually have to be repeated. The series of operations devised by Prof. Thiersch are the best in my opinion. First of all a penis must be made, as it is now a rudimentary affair, consisting of little more than a button, drawn up close to the pubes, the imperfect glans penis almost in contact with the hole which is directly over the deep urethra, and in contact with the pubes.

The first operation is to divide both corpora cavernosa subcutaneously, with a tenotome, close to the pubes. The penis is then drawn out and bound down with bandages for several weeks until it keeps more nearly to the normal position. After waiting for three or more months the second operation is done by sinking the urethra into the body of the glans and covering it in. Again a wait, when the third operation is performed by covering in the urethra on the shaft of the penis by superimposed skin flaps. The fourth procedure is to buttonhole the apron of skin below the glans, thrust the latter through it and fasten the edge of this new foreskin to the posterior margin of the glans and to the anterior edge of the new urethra in the shaft. After another wait, the last operation is done by closing the opening into the urethra close to the pubes by superimposed flaps, one of denuded skin, and one of skin only, from the pubic region.

In all these operations the difficult thing is to get the flaps to unite urine-tight, and without loss of substance. The last one is the most difficult to bring to a successful result. The final results in these cases, at best, are like the noses made by rhinoplastie operations, not beautiful; but we are thankful if they are useful, and the patient is able to hold his urine night and day instead of constantly dribbling, or losing urine on the slightest provocation, thus saturating his clothing, and making him unendurable to himself and to others. The increasing control of the sphincter with the successive operations until complete control is reached, is interesting.

A very clean operation, dry dressings, and a very faithful nurse are absolutely necessary to success.

The Relation of Cholelithiasis to Disease of the Pancreas and to Fat-Necrosis. DR. OPIE.

The patient whose history I shall relate was admitted to the service of Dr. Osler complaining of pain in the abdomen and fever. His family history is unimportant. He had suffered frequent attacks of indigestion characterized by pain after eating and, rarely, by nausea and vomiting. Six months before his fatal illness he had had an attack of jaundice which lasted three weeks and was accompanied by severe abdominal pain and some fever. The jaundice disappeared and he remained in good health until the beginning of this illness. He was suddenly attacked about nine o'clock one night with very severe abdominal pain followed by nausea and vomiting. The vomiting continued throughout the night but subsequently was not severe. The pain was great for about four days but became less severe. On the seventh day of his illness, tenderness and swelling appeared in the right hypogastric region. Jaundice was not noticed previous to his admission to the hospital. His temperature ranged between 100° and 103°.

He was admitted to the hospital on the eighteenth day of his illness and the note made by Dr. Fletcher shows that he was a large well-built man with a sallow complexion; the conjunctivæ had a very slightly yellowish tint. Examination of the chest was negative. On inspection of the abdomen a distinct prominence was noticed in the right hypogastric region extending into the right half of the umbilical with its lower margin at the level of the umbilicus. The urine at this time contained no sugar and its specific gravity was 1.017. His condition remained unchanged for two days, but on the night of the third day he became restless and delirious and his temperature rose gradually to 104°; the white blood-corpuscles numbered 19,500. The patient was transferred to the surgical side where the diagnosis of acute pancreatitis was made by Dr. Bloodgood and an operation was performed. An abscess was entered through an incision in the great omentum between the stomach and transverse colon. The cavity contained dark fluid, in which were necrotic particles. A drainage tube, packed about with gauze was inserted into the wound. There was a considerable amount of

discharge from the wound. The patient did not rally from the operation and died at the end of four hours.

An autopsy was performed a few hours after death. The skin surface was not jaundiced though the conjunctivæ had a yellowish tint. On opening the abdomen, the omentum, lightly adherent in the neighborhood of the wound, was found to contain a great quantity of fat. Studding this fat were conspicuous opaque white areas, about 3 mm. in diameter and extending below the surface not more than 1.5 mm. Similar areas were present in the fat of the mesentery, in that of the abdominal wall below the peritoneum over the bladder and in the fat in front of the kidneys. The preserved specimen here exhibited shows these areas of necrosis very well. The abscess which was entered at the time of operation was found to occupy the site of the lesser omental cavity and contained about 500 cc. of dark fluid in which were necrotic solid particles. Its wall was black and necrotic in appearance but on cutting into it the dark discoloration was found to extend only a short distance and gave place to opaque white areas of fat-necrosis. Projecting from the posterior wall of this cavity was a large projecting mass lying to the right of the descending portion of the duodenum, extending toward the spleen. It was composed of dark reddish-black material, was spongy in texture and suggested changed blood. The pancreas lay beneath it and was in large part well preserved. The gall-bladder contained a large number of faceted calculi (about 100) of an average diameter of 1 cm. In the common duct, 1.5 cm. from its origin, was a similar calculus. At this point the pancreatic duct was separated from the common bile-duct merely by a thin membranous septum, and it was upon this septum that the gall-stones lay.

Microscopic examination shows that the interstitial tissue of the pancreas is thickened and contains many cells in which are brownish-yellow pigment granules giving the reaction of iron. The necrotic material lying upon the surface of the pancreas is found to be changed blood. Cultures made from this necrotic material in the wall of the abscess were studied by Mr. F. H. Bassett; they contained the *Bacillus coli communis*, *proteus vulgaris* and *lactis aërogenes*.

The changes in the pancreas show that hemorrhage had occurred into and about the pancreas sometime before death. In the common bile-duct was lodged a gall-stone in such a position that it might readily compress the pancreatic duct and give rise to changes in the pancreas.

The relations of the pancreatic and common bile-duets are well known. They lie in contact for a distance of about 2 cm. and one can readily imagine that a gall-stone lodged near the orifice of the common duct might compress the pancreatic duct. In about two-thirds of all bodies the two duets of the pancreas anastomose within the gland, while in the other third there is no anastomosis, and should a gall-stone, lodged in the common bile-duct, compress the duct of Wirsung, the pancreatic accretion would be forced back upon the gland. When the common bile-duct is obstructed, the obstruction to the gall is readily shown by the yellow

color of the bile pigments which escape into the tissues, but when the pancreatic duct is obstructed the results are not so evident. Nevertheless, the condition of fat-necrosis gives evidence of the escape of the pancreatic secretion. The essential feature of this necrosis of fat is the splitting of the fat into its fatty acids and glycerin and numerous experiments have shown that if one produces a lesion of the pancreas which causes the pancreatic juice to escape into the tissues, necrosis of fat results.

In a series of experiments¹ performed upon cats, I ligated both ducts of the pancreas and at the end of about three weeks a very wide-spread necrosis of almost the entire abdominal fat, and to a less extent of the pericardial and subcutaneous fat as well, resulted. If, however, the ducts be ligated and pilocarpin be administered in order to stimulate the secretion of the gland, similar wide-spread necrosis occurs within four days, showing that the escape of the pancreatic juice is the essential feature. Where we find necrosis of the abdominal fat, we may assume that some lesion of the pancreas has allowed the escape of the fat-splitting ferment of the pancreatic secretion into the surrounding fatty tissue.

I have examined the literature of acute pancreatitis and fat-necrosis to determine the possible relationship of cholelithiasis to acute lesions of the pancreas, and I have found thirty-two cases in which such lesions were associated with the presence of gall-stones demonstrated by autopsy. Gall-stones, as is well known, are very frequently found at autopsy and may have caused no symptoms during life. It is therefore necessary to show that their presence bore some relation to the acute pancreatic lesion. In eight of the collected cases a gall-stone was actually lodged in the common duct near its orifice or had escaped from this position and lay in the duodenum. In five of these cases there were hemorrhagic lesions of the pancreas; the gland was enlarged and the interstitial tissue was infiltrated with blood. In the absence of microscopic examination it is impossible to say whether the lesion was a simple hemorrhage or a hemorrhagic inflammation. Four of the cases are particularly interesting, since death resulted within forty-eight hours from the onset of symptoms; the sudden onset of pain in the abdomen with nausea and vomiting was followed by collapse and death within forty-eight hours.

In three cases the symptoms noted above were followed by death within forty-eight hours. At autopsy the pancreas was infiltrated with blood; the gall-bladder contained calculi, but the one which had caused the fatal attack had escaped into the intestine and was not found. In one additional case a gall-stone had found its way into the duct of the pancreas.

There is another group of six cases in which the relationship of the pancreatic lesion to cholelithiasis may also be established. The duration of the fatal illness is longer and the symptoms are definitely those of gall-stone lodged in

the common duct; *e. g.*, pain and jaundice. At autopsy the diagnosis of gall-stone colic is confirmed by the presence of numerous calculi in the gall-bladder, but none are found in the ducts. It is not surprising that with the longer duration of the case the stone causing the trouble should have escaped into the intestine. In the former group it has been seen that a stone lodging only forty-eight hours might produce an intense hemorrhagic lesion. In these cases of longer duration there is usually evidence of previous hemorrhage; the organ is the seat of gangrenous inflammation and lies in an abscess limited to the lesser peritoneal cavity.

In fourteen cases the relationship could not be so definitely established. Though symptoms of gall-stone colic were present, the stone was not found lodged in the duct, nor was jaundice present. The changes in the pancreas resembled those in the previous cases, and it seems probable that in most of these cases the pancreatic lesion was a result of the lodgment of a gall-stone in the common duct near its orifice.

In twenty-six of the thirty-two cases fat-necrosis was present.

DISCUSSION.

DR. THAYER.—Two of the cases to which Dr. Opie has referred I reported ten years ago. The men had had repeated attacks of gall-stone colic and finally one very sharp attack with intense abdominal pain, sudden unaccountable collapse and death within forty-eight hours after the first symptoms. Autopsies showed acute hemorrhagic pancreatitis with, I think, evidences of older hemorrhages than those associated with the fatal attack, suggesting the possibility that with earlier attacks there had been some pancreatic trouble.

DR. WELCH.—By this communication Dr. Opie has added another valuable contribution to his important series of papers dealing with the histology and pathology of the pancreas. His previous experimental work has enabled him to come to a clear and satisfactory interpretation of his own and others' observations of the influence of gall-stones in the causation of various forms of pancreatic disease. Without this basis of experimental work this relationship of gall-stones to diseases of the pancreas could not have received so complete an explanation.

In this connection I wish to call attention to the importance of occlusion of excretory channels and ducts in favoring infection. This can be observed not only with the pancreatic and biliary ducts, but also with the urethra, ureter, salivary and other ducts opening upon exposed surfaces normally carrying bacteria. As Dr. Opie's experiments have shown, the damming back of the pancreatic secretion and its escape into surrounding and distant parts cause multiple fat-necroses and anatomical changes in the pancreas. Sometimes infection participates in these changes and modifies the conditions. The first recorded observation of the invasion of internal parts of the human body by the colon bacillus was the case of multiple fat-necrosis which I reported to the Association of American Physicians in 1890. In the class of cases considered in Dr. Opie's paper we have to

¹ Contributions to the Science of Medicine, dedicated to W. H. Welch, p. 859, 1900.

reckon in the first instance with the obstruction to the outflow of the pancreatic juice, and in the second place, as a frequently important factor, with the invasion of bacteria in consequence of such obstruction.

November 5, 1900.

Dr. Welch in the chair.

Secondary Syphilitic Eruption. DR. FUTCHER.

CASE 1.—The patient, a woman aged 34, was admitted on the medical side, October 17th, having previously been in the gynæcological ward since September 28th. Two weeks prior to her entrance into the hospital she had been complaining of pelvic pain, and after an examination the diagnosis of double salpingitis with a cystic ovary was made. The operation of vaginal puncture was performed October 1st and the cyst evacuated. I am indebted to Dr. Miller for permission to speak of the patient's condition while on the gynæcological side. She had had a slight fever previous to the operation, temperature going up to 101° , but contrary to expectation the temperature did not come down after operation but continued to rise until on October 3d it reached 103.2° . On that day she had a slight erythema of the skin and it was thought possible it might be some acute infectious disease. The following day Dr. Miller asked me to see the case with him but, though the eruption was still present, it was rapidly disappearing and seemed to have been nothing more than a temporary erythema. The patient was transferred, however, to the isolation ward to prevent any trouble in case our opinions should prove incorrect. The temperature then fell nearly to normal, being 99.2° on the morning of the 6th, but later the same day it ran up to 105.4° . In about 48 hours the temperature returned to normal and remained so for nearly 48 hours, when another paroxysm occurred, during which it reached 104.3° . It reached normal again in two days and she had another slight paroxysm which was followed subsequently by two other similar intermittent paroxysms.

The blood was examined on several occasions but no malarial parasites could be found. The leucocytes were repeatedly counted but there was no leucocytosis. Physical examination of all the organs was negative. We thought it might possibly be one of those obscure cases of Hodgkin's disease but there was no glandular enlargement. Her temperature now fell to nearly normal and continued so. The patient felt otherwise perfectly well and we allowed her to go home on October 23d.

On the 30th of October she came back with a perfectly typical macular, papular and pustular syphilitic rash on the face, arms and chest. Dr. Gilchrist was asked to see her then and diagnosed the case as one of secondary syphilitic eruption. I saw the patient yesterday and, the skin lesions still being present, I hoped to present the patient to-night. We found on investigating the history of the husband that he admitted exposure on July 4th, a primary sore on August 11th and a definite secondary skin eruption on August 28th,

so there seems little doubt that in this case the temperature which gave us a great deal of anxiety was due to the syphilitic eruption.

A word or two in regard to such fevers may not be out of place. In the first place, it may be of a more or less continuous type; secondly, it may be of a remittent type, the temperature not reaching normal but remitting towards the normal point; and thirdly—and these are the most interesting cases—it may be of the typical intermittent type resembling closely one of the forms of malarial fever. It may precede the secondary skin eruption, as in this case, but most commonly it occurs coincidently with the eruption. It may occur, however, during the course of either the secondary or tertiary symptoms; the most common time for it to occur is at the onset of or during the course of the eruption.

This case presents one of the unusual forms of intermittent type and it is also of interest in that the fever came on at least 27 days before the onset of the secondary skin eruption.

A somewhat similar case is reported by Yeo in the *British Medical Journal* for 1884. His patient had a fever with daily exacerbations ranging over 5 or 6 degrees. It was of a more or less continuous, persistent type, lasting for about one month. It occurred between 25 and 30 days after exposure and practically a month before the onset of the secondary skin eruption.

This fever of syphilitic origin may also occur late in the disease and Sidney Philips has reported a case that illustrated this very well. His patient was a young woman married in 1879. Six months later she had definite secondary symptoms and nine years subsequently developed a tertian type of fever which lasted almost eight months. The patient had definite chills at the onset of the paroxysms and profuse sweats followed them. The fever was not influenced by quinine but immediately disappeared on the administration of potassium iodide and mercury.

Case 2. In this case the cause of the fever is not so evident. A boy, 12 years of age, was admitted September 26th complaining of pain in the arms, legs and back of the neck. Five or six days previous to this he had a definite chill, which was followed by a fever that continued up to the time of admission. He looked well, but had a temperature of 104.2° , and the joints, particularly the knees and elbows, were reddened and swollen. There was also a considerable degree of stiffness of the neck, and the head was rotated to the left side. He did not have Kernig's sign, one of the important symptoms of meningitis. He was started on the salicylates and the next morning, his temperature having dropped to 96° , we thought possibly it was nothing more than a case of acute rheumatism. The temperature went up again the next day, however, and from that time on ran a very irregular course, remitting at times and at others being definitely intermittent. The leucocytes have been persistently high, ranging from 11,000 to 36,000. Lumbar puncture was done on two or three occasions but with negative results. Blood-

cultures taken at different times gave no organisms until last Saturday, when a coccus was found which has as yet not been identified. The boy has had repeated attacks of arthritis and at present there is some evidence of involvement of the apex of right lung. What the nature of the case is, it is difficult to say.

November 23, 1900. An interesting development occurred in this case on November 5th. On this date the highest temperature reached was 104.9° . The mere possibility of the fever being syphilitic in origin was entertained, and potassium iodide in 8 grain doses, three times daily, was commenced. The next day the boy's temperature reached normal and has remained so since. While we have not yet obtained any positive evidence of lues in the boy or his parents this therapeutic test is extremely suggestive.

DISCUSSION.

DR. OSLER.—The question of intermittent fever in syphilis is very interesting and was brought forcibly to our notice here by a remarkable case. An army officer was admitted with obscure symptoms after having been under treatment in other cities for some time. He had rise of temperature every day or every second day to 103° or 104° without any other symptoms. When he reached his ward the diagnosis was ready, however, as he had then developed the eruption.

Last year we had an interesting series of syphilitic fevers, several of them occurring quite early in the disease, one a markedly intermittent case and one a very continuous fever during the early stage of the disease.

Observations on Blood in Typhoid Fever. DR. THAYER.

(See Vol. VIII, No. XIX, Johns Hopkins Hospital Reports.)

DISCUSSION.

DR. WELCH.—The points brought out by Dr. Thayer concerning leucocytosis in experimental bacterial infections are particularly well illustrated in the infections of rabbits with *Micrococcus lanceolatus*, as I found several years ago when engaged in the study of this micro-organism. Every degree of virulence may be possessed by cultures of this micrococcus obtained from different sources. With maximum virulence of the organism and high susceptibility of the animal, death may follow experimental inoculation in 16 to 24 hours. In these cases there is progressive diminution in the number of leucocytes up to the time of death. With less virulent micrococci and greater resistance of the animal, death may be delayed for several days. There are then usually inflammatory exudates at the site of inoculation and often elsewhere, and now there is marked leucocytosis. Sometimes the animal survives notwithstanding evidence of severe infection, and in these cases I found the count of the leucocytes a valuable index to the probable issue of the infection.

Albumosuria. DR. HAMBURGER.

(To appear in a later number of the BULLETIN.)

November 19, 1900.

Exhibition of Pathological Specimens: Vegetative Endocarditis, Cystic Kidney, Carcinoma of Gall-Bladder. DR. MARSHALL.

The specimens I have to exhibit are a heart from one case and a liver and kidney from another. The heart specimen is particularly interesting. It is seen that two valves are affected, the mitral and the aortic. Upon examining the mitral valve, in addition to the fresh vegetations, one finds several firm, organized vegetations along the line of closure, and several of the chordæ tendineæ are ruptured and thickened. Attached to some of the chordæ are small nodules of dense fibrous tissue. From this condition it is evident that there has been a former attack of acute endocarditis from which the patient has recovered.

There are no old vegetations on the aortic valve or on the ventricular surface of the mitral valve.

The largest of the fresh vegetations are on the ventricular surfaces of the posterior and left cusps of the aortic valves. These vegetations have been somewhat injured in preparing the specimen, but at the autopsy they formed a mass projecting about 2 cm. from the under surface of the valve. At the base of the vegetation is a large ulceration through the left aortic leaflet. From this most prominent lesion, a row of small fresh vegetations extends up into the sinus of Valsalva, and also down over the ventricular surface of the mitral leaflet to its free border. A few small recent vegetations are also present along the line of closure of the mitral valve.

From the extent of the lesion on the aortic valve, and from the fact that the vegetations grow fewer and smaller the further they are situated from the aortic valve, it seems probable that the acute endocarditis started on the aortic valve.

In addition to the chronic and acute valve lesions there is general cardiac hypertrophy and dilatation, and adherent pericardium, and, finally, a moderate degree of fibrous myocarditis.

It may be noted that the orifices of the heart are of smaller circumference than normal:

The aortic orifice measuring	6.5 cm.
The mitral orifice measuring	9.0 cm.
The pulmonary orifice measuring	8.5 cm.
The tricuspid orifice measuring	12.0 cm.

Dr. Harris found streptococci in coverslip preparations and in cultures from the fresh vegetations, and in sections stained by the Gram-Weigert method masses of cocci can be seen at the edge of the vegetations. Nothing more of interest was found at autopsy. No infarcts were discovered.

The most important recent work upon endocarditis that I have found is by Harbitz in the *Deutsche medicinische Wochenschrift*, 1899, No. 8, S. 121-124.

He divides the endocarditides into infectious and non-infectious, the latter associated with carcinoma or other cachectic conditions.

Out of 43 cases of infectious endocarditis, Harbitz demon-

strated bacteria in 33, the relative frequency of various organisms being:

Streptococci	39.5%	17 cases.
Staphylococci	18.6%	8 "
Pneumococci	11.6%	5 "
Other organisms	6.9%	3 "
No organisms	23.2%	10 "

The 10 cases without organisms were cases of healed infectious endocarditis, such as is seen on the mitral valve of the specimen shown to-night.

Harbitz subdivides the infectious endocarditides into pyæmic and non-pyæmic. He finds that the staphylococci most often cause pyæmic endocarditis, giving the clinical picture of pyæmia and, anatomically, showing ulceration of the valves and metastatic abscesses.

The non-pyæmic variety is usually due to the streptococcus or pneumococcus. Of his 16 cases of this form of endocarditis, in 9 Harbitz found streptococcus, in 4, pneumococcus and in 2, an unidentified organism.

In this group of cases the disease may last longer, and the vegetations tend to be larger and to spread into the auricles and ventricles. The emboli are not suppurative. Harbitz does not consider this classification absolute, but states that the same organism may produce any type of endocarditis, from the mild vegetative to the pyæmic, ulcerative form.

The specimen shown to-night conforms more closely to Harbitz's non-pyæmic type of endocarditis; the vegetations show the streptococcus, they are very large, they tend to spread quite widely, and there are no suppurative emboli. The specimen approaches Harbitz's pyæmic type in showing ulceration of the aortic valve.

The other two specimens shown to-night are from an autopsy performed a few days ago at Bayview. One is a congenital cystic kidney, the other carcinoma of the fundus of the gall-bladder, with metastases to the adjacent surface of the liver and to the lymph-glands along the bile-ducts.

DISCUSSION.

DR. WELCH.—Dr. Marshall has referred to the interesting observations of Harbitz of Christiania, who distinguishes *Staphylococcus endocarditidis* from those caused by streptococci, pneumococci and other bacteria. According to Harbitz, staphylococci are the principal infectious agents in acute ulcerative endocarditis, whereas the other micro-organisms cause the more chronic and warty forms of endocarditis with non-suppurating infarcts, these latter forms being the more common.

It would be interesting to analyze our cases with reference to this classification of Harbitz. When some years ago I went over our autopsy-protocols, I found that streptococci first and pneumococci in the second instance were most frequent in endocarditis, but staphylococci were occasionally met, and in addition there is quite a long list of other bacteria sometimes present in the vegetations, among the latter, gonococci, *Micrococcus zymogenes* of MacCallum and deli-

cate, slender bacilli resembling the influenza bacillus being of especial interest. I do not recall that staphylococci were responsible for peculiarly malignant types of the disease, and certainly streptococci were present in some of the instances of genuine ulcerative endocarditis. The efforts to associate definite species of bacteria with the various clinical and anatomical types of endocarditis have upon the whole yielded disappointing results, the same micro-organisms being found in the milder warty forms of the disease as in the acute ulcerative varieties. In the light of Harbitz's conclusions it seems important to continue the studies along these lines. One point is of interest, viz.: that emboli containing streptococci may cause bland, or at least non-suppurative infarcts.

Congenital Absence of Pectoralis Major and Minor. DR. RUSK.

(To appear in a later number of the BULLETIN.)

Report of Gynecological Cases. DR. MILLER.

CASE 1.—*Simple Ulcerative Colitis*.—I intended to report this case because I thought I had cured it by applications to the lower part of the bowel, but since the program was printed I have had occasion to examine her again and find that the ulcers have returned. The patient was a young woman, 25 years of age, who about 14 months ago began to complain of diarrhœa. She had no nausea or vomiting but the bowels were moved from six to twelve times a day, the stools being dark-colored and offensive. Her mother and several other persons in the neighborhood who use the same drinking water were affected in somewhat the same way although not so severely. She was treated in the usual way and, according to her statement, was kept in bed for about six weeks, receiving medicines by the mouth, and irrigations. She would improve somewhat but as soon as she got on her feet again the diarrhœa returned.

She entered the hospital September 4th and was examined by Dr. Hunner, the patient being placed in the knee-chest position and the bowel examined by means of the long speculum. Examinations for ameba proved negative. Numerous ulcers were found and the cultures from these gave a great variety of bacteria but nothing characteristic. A curetting was done and the debris examined under the microscope but without showing anything very definite.

Dr. Hunner has drawn here a description of some of the ulcers as seen at the first examination. They were horse-shoe-shaped, about 2 cm. from one end to the other and about 5 or 6 mm. across the narrow portion with a granular-looking base and very little congestion in the neighborhood. In his description of the findings it was noted that there was marked congestion extending up to the sigmoid. The areas of involvement had very much the appearance of ringworm.

The patient was put to bed, given a milk diet, and silver nitrate irrigations were administered in varying strength. After a month of this treatment without improvement the patient was placed in a knee-chest position, the speculum inserted and a piece of iodoform gauze saturated in a 10 per cent ichthyol solution was placed in the bowel and allowed

to remain one hour. After the first application she had a number of stools, but on the following day had them only after the irrigations. After about six applications she had no stools except those following applications or irrigations, and an examination of the rectum showed that the ulcers had disappeared. On Wednesday last, Dr. Kelly saw her again and found a few small ulcers, and when I examined her again to-day I found her condition to be almost as bad as at first. We shall continue the same treatment and report results later.

CASE 2.—This case presents simply a rather unique way of dealing with large oozing raw surfaces where the intestines might become adherent and cause trouble. The patient, a woman aged 60, entered the hospital October 19th with a large tumor in the left side of the pelvis. The diagnosis was made of a possible carcinoma of the left ovary with adhesion of the structures around it. An incision was made and a large tumor was found springing from the left ramus of the pubes. It was not connected in any way with the ovary or tube and examination proved it to be a fibroma. We tied off a good many of the blood-vessels coming from the abdominal walls and tried to cut through the capsule of the tumor in order to shell it out. In trying to do this on the right side the scissors entered an open space, apparently in the capsule, but instead we incised the bladder for about 8 cm., making a triangular cut. The tumor was finally enucleated and it left the whole anterior part of the pelvis a raw surface. This raw surface in front of the uterus could not be covered with peritoneum, and it was a question at first how to cover it so as to prevent the intestines becoming adherent. We began on the left side and sutured the round ligaments up to the anterior abdominal wall and then the uterus was stitched to the wall by interrupted sutures. The same plan was carried out on the right side and, after closing the bladder wound, the oozing area was packed with gauze. In this way the abdominal cavity was cut off entirely from this oozing space in front of the uterus. The result justified the means, because the patient recovered without any serious complications.

Demonstration of a New Hemoglobinometer. DR. ARTHUR DARE, Philadelphia.

Through the kindly interest manifested by Professors Flexner and Hare, I have the honor of presenting a new instrument for estimating the quantity of hemoglobin in blood by an improved means. The application of the instrument differs from that operative in the popular instruments of Von Fleischl, Gowers and Oliver, by using blood unmixed with artificial serums. The method consists in ascertaining the percentage of hemoglobin by comparison of the color of the blood arranged into a thin film of measured thickness with a fixed standard color equally illuminated by transmitted candle-light.

The essential parts of the instrument are an automatic pipet for collecting the blood, and a graduated color comparison to measure the percentage of hemoglobin therein

contained. The pipet for collecting the blood is composed of an oblong plate of white or opal glass, into the end of which is ground a depressed surface exactly parallel with its plane surface, and of measured depth. This depression forms a very shallow capillary chamber when the transparent glass is placed over it and the two are clamped tightly together with a pipet-clamp. This space fills automatically by capillary attraction when either of the three free edges is touched lightly to the blood drop. When filled the pipet is placed upon the stage of the instrument and held in position by grooves, and is then compared with a color comparison composed of a semicircle of tinted glass, the periphery of which represents an increasing shade of color from apex to base. This is secured to a disc of opal glass which serves the same purpose as in the pipet, disperses the light and furnishes a white background against which the color shades are best appreciated.

The blood and comparison placed horizontally side by side are viewed through achromatic lenses fitted into the telescoping camera-tube, and the comparison adjusted by means of a milled head, which in turn rotates the color prism until the same corresponds in color with the blood. The operation is completed by noting the percentage of hemoglobin indicated.

As the examination only consists of filling the pipet and comparing the color shade with the comparison, the time required for an observation is reduced to the minimum of 1 or 2 minutes, which places hemoglobin estimation among the practical clinical methods.

We will consider the instrument from the aspect of the scientific hematologist.

By using a stratum of blood the thickness of which is always constant, we avoid the volumetric character of all dilution methods. It is evident that if the ends of the column of blood contained by the pipet are either concave or convex, or if the outside is soiled, an error must result.

As the blood film is viewed against an illuminated white background, leucocytosis is imperceptible; only the red color of the hemoglobin is visible.

With the Fleischl the error due to leukocytosis is considerable, as the blood and water mixture is turbid, and does not compare with the clear tone of the color comparison, making the readings low, while in leukopenia they are high.

Again, by using undiluted blood we avoid the dilution color curve; to illustrate, an equal volume or weight of normal 100 per cent blood and water, instead of reading 50 per cent reads 65 per cent; this discrepancy is the color curve. In every different sample of blood which is an intravascular dilution, we have a color curve due to different degrees of hemoglobin concentration; this color curve is likewise adjusted by keeping an equal concentration of coloring matter in the blood film and color comparison; *e. g.*, blood reading 100 per cent requires greater concentration of color, hence a thicker stratum of colored glass to give an equal shade, than a film containing 20 per cent of hemoglobin.

We keep the focal distance of all observations uniform by using achromatic lenses and a fixed camera-tube and obtain a large field from apertures that cover only 3 per cent of the comparison disc, against 20 per cent in the Fleischl. We also have darker shades to compare, an operation less difficult than with delicate tints.

The instrument can be used in daylight by directing the line of vision toward a dark surface, as a black coat that does not reflect light. I frequently use it in the hospital wards where the brightness of daylight is intensified by the whiteness of walls and linen.

If the colors do not look alike daylight either direct or reflected is entering beside the candle flame, the yellow light of which only in a measure occludes the violet rays of the solar spectrum.

Five hundred comparative examinations with the instruments of Von Fleischl, Oliver and this instrument show readings always very close to the Oliver.

With the Von Fleischl the results are at variance in low hemoglobin percentages, in leukemic blood and in blood showing leukocytosis.

As it is occasionally desirable to keep the blood in the pipet fresh a long time a special pipet is made that protects the edges of the blood film from exposure to air, except at two minute points, which are provided for capillarity. This is not so readily cleansed but is convenient for demonstration.

In testing the various methods available with undiluted blood, viewing the blood film and color comparisons placed side by side by doubly reflected light (as is used in the Oliver instrument) was finally abandoned for the much more satisfactory method of illumination of the blood as the most perfect means of color analysis.

An attempt was also made to estimate the hemoglobin through the ear-lobe by illumination with a greater degree of success than would at first seem possible.

In conclusion, I desire to point to the practicability of the instrument. The application requires but 1 or 2 minutes, and no special technical skill to operate. Accuracy is not sacrificed to celerity; on the contrary the results in successive trials are constant and more uniform than with dilution methods.

In testing the instrument with the view to determining the degree of variations known to exist in colorimetric observations with other instruments, experiments were made with clinical patients whose knowledge of the instrument only extended so far as being able to arrange the colors until the tone agreed; variations of more than one or two per cent were very infrequent; with shop girls, accustomed to the matching of color shades, the readings were still more uniform, points that class it as a most valuable instrument of precision.

I would also call attention to the blood-lancet that accompanies the instrument. A bayonet-pointed needle is held by a simple chuck mechanism to any desired length from the hard-rubber guard fixed or released by a turn of the metal

collar. The needle can be removed for sterilization or replaced by another needle in case the point is damaged or corroded.

December 3, 1900.

In the absence of the president, Dr. Jacobs in the chair.

Cirrhosis of the Stomach. DR. McCRAE.

Dr. Osler is unavoidably absent this evening, and as he would probably prefer to report personally one of the cases he had intended showing this evening, I will merely present the specimens from the other case.

The case is supposed to be one of cirrhosis of the stomach, a rare condition. Unfortunately, Dr. Osler has notes of the case with him and I can only speak from my own recollection of them. The patient was about 48 years of age and his symptoms began about five years ago in a rather sudden way. It is curious how many patients complain of acute gastric trouble beginning after a period of overheating and the drinking of cold beer. Such was the history in this case. The patient gradually lost weight for some time though he did not suffer from nausea or vomiting. About a year ago he came to the hospital and his case was diagnosed as one of carcinoma of the stomach. He had then considerable emaciation, moderate anæmia and a slight ridge in the abdomen with a sense of resistance but no definite tumor. There was absence of free hydrochloric acid and the presence of lactic acid.

About two months ago he consulted Dr. Osler. His history was practically the same as before with one additional symptom, namely that in the last year he had been able to take only a definite small amount of nutriment at one time, becoming nauseated whenever he exceeded this quantity, and, that small amount was decreasing constantly. He had then lost over 100 pounds in weight. The test meal, which we finally succeeded in getting, was rather unusual in that it showed 90 per cent of fluid, a total acidity of only 10 and the total absence of free acids. Upon the long duration of the case and the above history, Dr. Osler based his diagnosis of cirrhosis of the stomach.

Dr. Finney, at the operation, found practically an hour-glass constriction of the stomach. An opening was made in the stomach-wall and at first it was impossible to pass a finger beyond the stricture. A small probe was used, then a larger one and so on until finally two fingers could be passed and the stricture was then dilated. The wound was closed in the usual way but the patient did not do well, gradually sank and died four days later, apparently from inanition.

The specimen is here. Sections removed at the time of operation show a great overgrowth of tissue and no sign of malignant disease or of previous ulcer. Cirrhosis ventriculi is a rare condition and the diagnosis is rarely made during life with any degree of certainty.

Abdominal Tumor containing a Dermoid Cyst. DR. MITCHELL.

The case was one of a young man, 34 years of age, who gave a history of the presence of colicky pains in the abdo-

men during the past ten years. During the past five years these pains have increased in severity. Three years ago he first noticed a tumor about three or four inches just below the umbilicus, and under the impression that it was a floating kidney, an exploratory incision was made to-day, and a dermoid cyst in the mesentery of the ilium was found. (A fuller account will be published later.)

DISCUSSION.

DR. FUTCHER.—In regard to the question of diagnosis of this case, the possibility of its being other than a displaced kidney was entertained. Dr. Osler, as well as Dr. Finney, spoke of the possibility of its being a mesenteric tumor or a tumor in connection with the bowel but it seemed to conform more to the general character of a floating kidney, although its shape was not exactly that of a normal kidney. Personally, I thought it was a displaced kidney, but Dr. Osler was rather non-committal. Dr. Young made a cystoscopic examination and found the flow of urine from the two ureters to be normal. This should have impressed us more strongly than it did as to the probability of its not being a kidney tumor.

DR. BLOODGOOD.—There have been three other dermoids on the surgical side during the last ten years, although very few tumors of the mesentery itself. Two of the dermoids were in men of about 30 years of age and the patients had not been aware of their existence for any length of time. Both were opened and drained. Both were behind the peritoneum and the autopsy on one proved that the tumor could not have been removed. The third cyst was, I think, in practically the same location as in the case reported by Dr. Mitchell, but it was adherent to the bladder and was associated with attacks of hematuria. It was demonstrated later that a carcinomatous growth had been engrafted upon the cyst.

Two Cases of Acute Pancreatitis. DR. BLOODGOOD.

The first case has been reported by Dr. Thayer and the second is a recent one that Dr. Mitchell and I saw together with Dr. Fletcher. The disease is so rare that I think the few of us fortunate enough to see it should be good enough to bring it before the majority. The diagnosis is not often made, but I believe an early diagnosis followed by operation would in the majority of instances be followed by recovery. In the last ten years we have had some 12,000 surgical admissions to this hospital and probably as many more on the medical side, but we have only seen in all that number three cases of pancreatitis; one hemorrhagic and two suppurative. As I had had the good fortune to see the first case the diagnosis of the second was not difficult.

The patient was a physician, 47 years of age, whose only previous illness consisted in symptoms of indigestion with pain after eating associated with slight distension and rarely nausea and vomiting. Seven months previous to his last attack he had with one of these spells a condition of jaundice which lasted three weeks. The onset of the last attack, 18 days before coming to the hospital, was sudden and asso-

ciated with nausea, vomiting and intense cramp-like pains all over the abdomen. After five days of this, his abdomen was slightly distended but there was no area of tenderness. The vomiting was worse during the first 24 hours and only present at intervals after that. On the third day his temperature was high, for the first time reaching 101.5°. On the seventh day his physician noticed a mass in the right lumbar region but he does not give the location very definitely. He then began to have irregular fevers and chills and throughout the entire attack the abdominal pains were present but not very marked except during the first day. There was no jaundice.

The tumor was visible only to the right but was palpable some distance to the left of the median line. There was a leukocytosis of 19,300. The patient remained under observation for three days with very little change in his condition except that he was growing weaker and slightly delirious. When I saw him he was in a toxic condition and looked very ill. The surface over the tumor was very irregular, like that of the omentum around an acute appendicitis. The mass was large and immovable at that time and all around the tumor a tympanitic note was obtained on percussion. The position of the tumor corresponded with that of the first and was different from that of appendicitis or other tumors in the abdomen.

At the operation, performed under cocaine, there was found to be a great deal of fat and the omentum was studded with areas of fat-necrosis. The tumor was adherent to the parietal peritoneum, and a tendency to bleed was noticed but there was no hemorrhagic area. The mass under the omentum was hard and everything about it bled easily when separated. For that reason the knife was not used but the fingers were employed to separate the parts. When pus was found it was first yellowish and then of a deeper brown color like chocolate. There were at least 250 cc. and it seemed to come from numerous pockets. The man died within 12 hours after the operation, which seemed to have no particular effect on his condition.

DISCUSSION.

DR. OPIE.—In Dr. Bloodgood's case the autopsy showed an abscess occupying the site of the lesser peritoneal cavity. The incision made at the operation passed through the greater omentum between the stomach and transverse colon and the drainage tube entered a large cavity lined with necrotic fat. The tumor mass felt during life was not the pancreas but spongy brownish-red material which lay in front of it and on examination proved to be changed blood. The orifices of the common duct and pancreatic duct were separated by a thin membrane; a gall-stone was lodged in the common duct near its orifice in contact with this membrane and therefore in such position that it could compress the pancreatic duct. The pancreas was the seat of beginning chronic interstitial inflammation and there was evidence that hemorrhage had occurred into and about it. In thirty-one reported cases I found that acute lesions of the pancreas

have been associated with the presence of gall-stones, and in seven of these cases a stone occupied a position similar to that just described. In four of these seven cases the symptoms were very acute, and death occurred within 48 hours; the autopsies showed infiltration of the pancreas with blood. It is difficult to say whether the condition was a simple hemorrhage or a hemorrhagic inflammation. It seems probable that in this case the stone lodged in the common duct occluded the pancreatic duct. As the result of subsequent changes hemorrhage occurred into and about the gland. The patient survived the primary lesions and thus gave opportunity for secondary infection resulting in a peri-pancreatic abscess.

Tuberculosis of the Aorta. MR. LONGCOPE.

The patient was a colored child admitted to the Johns Hopkins Hospital November 9, 1899, and a diagnosis of tuberculosis of the hip was made. On examination the heart and lungs were found normal. The cervical lymph-glands were palpable. On November 11th an incision of the sub-



FIG. 1.—Small tubercles at the margin of the necrotic mass. The section is from the lower end of intima.

gluteal abscess and arthrotomy were done. The wound healed well and the child remained in good condition until January 10, 1900, two months after the operation, when a cough was noticed. A few days later on, January 20th, the child's temperature, which had been practically normal, rose to 103° , and an examination of the lungs showed patches of consolidation in the left apex and both lower lobes. From this time the patient's temperature was more or less elevated and occasionally reached 104° . The patient grew steadily weaker and died on March 3, 1900, almost four months after the operation.

The anatomical diagnosis made at the autopsy reads—*Tuberculosis of the hip; abscess formation in the muscles anterior to the acetabulum; chronic tuberculosis of the right*

lung; miliary tuberculosis of the lungs, liver and spleen; acute splenic tumor; hyperplasia of the lymphatic glands and lymphatic tissue in the intestines; mural thrombus of the aorta.

The chronic tuberculosis of the right lung consisted in a caseous patch about 5 cm. in diameter at the apex of that lung. Although the kidneys showed no distinct tubercles macroscopically, still on microscopic examination aggregations of epithelioid and lymphoid cells were found which strongly suggested tubercle. The thrombus was situated on the posterior wall of the lower abdominal aorta, and consisted of a polypoid projection about 3 cm. in length, bent downwards and closely hugging the wall of the aorta. At its lower extremity a fresh red thrombus mass was attached.

A section of the lesion in the aorta shows that the nodule is composed of a mass of necrotic granular material, containing no cell elements. It is surrounded, except at its lower extremity, by intimal tissue, and presents much the appearance of an ordinary atheromatous plaque. On close examination, however, the lining intima is found to contain epithelioid and lymphoid cells which at its lower extremity arrange themselves into two definite tubercles containing giant cells (Fig. 1). About the periphery of the necrotic granular material and beneath the intimal border are seen masses of fibrin. Near the intima the fibrin is continuous with radially placed cells of an epithelioid type. The necrotic mass itself contains great numbers of tubercle bacilli, which stain with carbol fuchsin, and are not decolorized after treatment with 10 per cent nitric acid for half an hour. These bacilli also stain well in alkaline methylene blue. The entire lesion of the intima, then, must be considered a chronic tuberculosis with marked caseation.

The media, on the other hand, presents a different picture. Directly beneath the lesion in the intima, masses of lymphoid and epithelioid cells with a few giant cells are seen in the media. There is no definite arrangement of these cells suggestive of tubercle. At one point the growth in the media and the caseous mass in the intima are separated only by a few elastic fibres, but in greater part the lesion is confined to the middle portion of the media. Numerous blood-vessels are seen running through the diseased portion. Weigert's elastic fibre stain shows that the elastica has been greatly damaged. The tuberculous process has broken the elastic fibres into small pieces which appear as short curled threads. The lesion occupying the mid portion of the media pushes outward, and at its margins widely separates the elastic fibres next the adventitia. These fibres are often broken and their ends sharply bent outward. In no place does the growth in the media extend into the adventitia, and, except for increased vascularity and slight thickening, this coat appears practically normal.

Few cases of tuberculous aortitis have been reported; whereas tuberculosis of the veins and smaller arteries seems to be of comparatively frequent occurrence. In 1882, Weigert, in an article on tuberculosis of the veins in Virchow's Archives, describes two cases of miliary tuberculosis of the aorta which Marchand and Huber showed him. In

the same volume of the Archives Schuchardt mentions a case of miliary tuberculosis of the abdominal and thoracic aorta occurring in a case of general miliary tuberculosis. Eight subsequent cases have been reported in Germany and France by Dittrich, Hanot, Kamen, Hanot and Lévy, Hanau and Sigg, Buttermilch and Benda; and three cases in America, one by Dr. Flexner, a second by Dr. Blumer, and Dr. Welch, in his article on Thrombosis and Embolism, mentions a third case shown to him by Dr. Gaylord.

These fourteen cases can be divided into two groups: those in which there is a primary tuberculosis of the intima caused by a direct deposition of the bacilli from the blood stream, upon the endothelium of the aorta; and those in which the adventitia is the seat of primary invasion with an extension of the process into the media and intima. Ten of the fourteen cases belong to the first group, and in this group also the present case should be included. In all the cases of this group of primary infection of the intima, except that reported by Stroebe, the tubercles were either miliary or exceedingly fresh. In Stroebe's case, however, a caseous polyp surrounded by epithelioid cells was found projecting from the intima of the ascending aorta. This polyp was capped by a thrombus mass. The present case closely resembles that of Stroebe.

Of the four cases of group II, the primary involvement of the adventitia occurred in the following manner: Twice, *i. e.* in the cases of Dittrich and Kamen, a caseous lymph gland was found adherent to the adventitial wall of the aorta, and the tuberculous process could be traced directly from this focus into the media and intima. Hanau and Sigg describe a portion of a tuberculous lung adhering to the arch of the aorta. A small aneurysm of the aortic wall projected into a tuberculous cavity of the lung. The aneurysm was filled with a thrombus mass. Tubercle bacilli were found in the thrombus and artery wall. In the fourth case of this group Buttermilch traced the aortic tuberculosis from a chronic tuberculous focus in the thoracic vertebræ. The aorta and vertebræ were firmly adherent, and small caseous abscesses were found in the adhesions.

In connection with the present case it is interesting to note Benda's views concerning the part played by tuberculosis of the blood-vessels in general miliary tuberculosis following operation or injury of tuberculous joints and bones. In three of such cases he finds tuberculosis of the blood-vessels, and he believes that during the operation or injury a few bacilli make their way into the circulation and lodge upon the intima of some blood-vessel, thus forming as it were a tuberculous metastasis. At this time there is no general invasion of the bacilli. In the intima of the vessel a tubercle develops, becomes caseous and finally ruptures, liberating great numbers of tubercle bacilli into the circulating blood. These bacilli are distributed throughout the body and are the direct cause of the general miliary tuberculosis.

Since in the present case the aortic tuberculosis is the only chronic process except the focus in the right lung, it

is not impossible that the general miliary tuberculosis may have been directly caused by the rupture of the caseous tubercle of the intima.

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NOTES AND NEWS.

Dr. John S. Billings, Jr., Assistant Resident Physician at the Hospital during 1892, '93 and '94, resides at 32 East 53rd St., New York City. He is Assistant Director of the Bacteriological Laboratory of the Department of Health, having resigned his position of Instructor in Clinical Microscopy in the University and Bellevue Hospital Medical School.

Dr. C. N. B. Camac, Assistant Resident Physician at the Hospital during 1896, '97 and '98, resides at 108 East 65th St., New York City. He is Visiting Physician to the City Hospital, and Instructor in Clinical Pathology at the Cornell Medical School.

Dr. E. P. Carter, Assistant Resident Physician at the Hospital in 1894 and '95, resides at 8 Hayward St., Cleveland, O. He is Lecturer on Medical Jurisprudence in the Western Reserve University Medical School, a member of the staff of the City Hospital, and an Assistant in the Out-Patient Department of the Lakeside Hospital.

Dr. Edmund D. Clark, Assistant Resident Surgeon at the Hospital in 1895, resides at Indianapolis, Ind. In 1896 he was appointed Demonstrator of Histology in the Medical College of Indiana; in 1897, Adjunct Professor of Physiology and Surgical Pathology; in 1898, Consulting Surgeon of the City Hospital, and in 1899, Instructor in General Surgery at the Protestant Deaconess Hospital.

Dr. George Edward Clark, Assistant Resident Surgeon at the Hospital in 1889 and 1890, resides at Skaneateles, N. Y.

Dr. John G. Clark, Resident Gynecologist at the Hospital in 1895 and '96, has been appointed Consulting Gynecolo-

gist to the Woman's Hospital, Philadelphia. He resides at 218 South 15th St.

Dr. Malvern B. Clopton, Assistant Resident Surgeon at the Hospital in 1898, resides at 3732 Olive St., St. Louis, Mo., and is connected with the Medical School of the Washington University.

Dr. Theo. Coleman, Assistant Resident Surgeon at the Hospital in 1895 and '96, who now resides at 569 Spadina Ave., Toronto, Ont., has been appointed Head Surgeon and Physician to the Canadian Copper Company, at Copper Cliff.

Dr. J. Colton Deal, Assistant Resident Obstetrician at the Hospital in 1898, resides at 5301 Haverford Ave., Philadelphia. He is Pathologist to the Gynecological Department of the Polyclinic Hospital.

Dr. George W. Dobbin, Assistant Resident Obstetrician at the Hospital from 1894 to '97 and Resident Obstetrician from 1897 to '99, has been appointed Professor of Obstetrics in the College of Physicians and Surgeons of Baltimore. He resides at 923 N. Charles St., Baltimore.

Dr. W. W. Farr, Assistant Resident Gynecologist at the Hospital in 1890 and '91, resides at 5728 Greene St., Philadelphia, Pa.

Dr. McPheeters Glasgow, Assistant Resident Gynecologist at the Hospital in 1896 and '97, resides at 151 N. Spruce St., Nashville, Tenn., and is connected with the Vanderbilt Medical School.

Dr. Francis R. Hagner, Assistant Resident Surgeon at the Hospital in 1896, resides at 1717 N St., Washington, D. C. He has charge of the Surgical Dispensary at the Garfield Hospital, and is Instructor in Bacteriology at the Columbian University Medical School.

Dr. Hunter Robb, Resident Gynecologist at the Hospital from 1889 to 1894, resides at 1342 Euclid Avenue, Cleveland, O. He is Professor of Gynecology at the Western Reserve University, and Gynecologist-in-Chief to the Lakeside Hospital.

Dr. Chauncey P. Smith, Assistant Resident Surgeon at the Hospital in 1893 and '94, resides at 90 N. Pearl St., Buffalo, N. Y.

NOTES ON NEW BOOKS.

Cancer of the Stomach: A Clinical Study. By WILLIAM OSLER, M. D., and THOMAS McCRAE, M. B. (Tor.), of the Johns Hopkins Hospital, Baltimore. With illustrations. (Philadelphia: P. Blakiston's Son & Co., 1900).

The prevalence of cancer of the stomach, and the value to the physician of a thorough knowledge of the clinical features of the disease, as well as the importance to the patient of its early recognition, makes this admirable monograph a welcome acquisition to our literature on the subject.

The monograph contains 157 pages with several illustrations in the text. It is essentially a critical study of 150 cases of primary cancer of the stomach admitted to the Johns Hopkins Hospital from its opening, May 5, 1889, until March 31, 1898. Of these, 2 were instances of multiple primary cancer. During the same period 3 cases of secondary cancer of the stomach

came under observation, and these are considered separately. The literature has been carefully examined and much additional information thus added.

The authors believe there is evidence that cancer in general is on the increase. They hold, however, that there is not sufficient proof at hand to warrant the same conclusion concerning cancer of the stomach. The general etiology of the disease is then taken up. The ratio of the disease in males and females was 5 to 1. The greatest number of cases occurred in the fifth decade. The white and colored race are apparently about equally liable. The ratio of the disease in the two races was respectively 6.9 to 1. The ratio of admissions is 6 to 1. In only 6 cases was there a family history of cancer. There was a history of ulcer of the stomach in 4 cases. Trauma seemed to bear a causal relationship to the onset of the disease in only one instance.

An interesting chapter is devoted to cancer of the stomach in the young. The writers give 30 years as the convenient dividing line below which cancer of the stomach may be considered as occurring in the young. They have collected from the literature 6 authentic cases in the first decade and 13 in the second. The number of cases which are reported as occurring in the third decade is much larger and forms an interesting group from the standpoint of diagnosis. All their cases below 30 were in the third decade, the youngest patient being 22 years of age. There were 6 cases, or 4 per cent of the total, in this decade, and they consider this number unusually large. An important feature of the disease in the young is its rapid progress.

General instructive chapters are devoted to an analysis of the symptoms present in the 150 cases. An interesting feature was the surprisingly large number of patients who gave a history of an acute onset. There were 37 cases in which the onset could be termed sudden. The three most constant symptoms were pain, vomiting and tumor. Pain occurred in 130 cases, or 86.6 per cent.; vomiting in 128 cases, or 85.3 per cent.; tumor in 115 cases, or 76.6 per cent. In 87 cases in which stomach contents were obtained for examination, there was an absence of free hydrochloric acid in 80, or 92 per cent. There were seven cases in which free hydrochloric acid was found. In the series, lactic acid was examined for in 73 cases and was found present in 55, giving 75.3 per cent. The writers consider that Uffelmann's test for lactic acid is satisfactory, laying stress on the fact that an ethereal extract should be used in making the test.

Certain associated and secondary symptoms are then taken up. Perforation into the peritoneal cavity or adjacent portions of the intestinal tract occurred in 6 cases. In 2 cases there were secondary metastases at the umbilicus. Jaundice was present in 6 and ascites in 8 cases. Thrombosis of the left femoral vein occurred in 2 cases. Thrombi were found post mortem in 3 cases. There was one remarkable case in which thrombosis of fourteen or fifteen veins was found.

Some of the most interesting chapters are devoted to the study of the different features associated with the site, shape, structure and character of the tumor, which was made out in 115 cases. The importance of inspection of the abdomen is emphasized. In 42 cases the stomach was dilated, the dilatation in each case being visible to the naked eye. The atrophic form of carcinoma ventriculi was present in 12 cases, and was recognized in 6 during life.

A chapter is devoted to the blood in cancer of the stomach. It is rather disappointing to find that in the cases in which the blood was examined for a digestion leucocytosis, the absence of such a leucocytosis was not by any means a constant feature. In 22 cases thus examined it was present in 10 and absent in 12. They are inclined to the opinion that little reliance can be placed on the digestion leucocytosis from a diagnostic standpoint.

The disease was latent in 8 cases and was unsuspected during life. Autopsies were obtained in 46 cases. The following figures give the frequency of involvement of the various regions of the stomach: Pyloric region, 24; general involvement, 6; lesser curvature, 5; greater curvature, 3; cardia, 3; posterior wall, 3; fundus, 1.

The monograph concludes with the therapeutic management of the disease. The medical treatment is palliative and is intended for those cases which are beyond surgical interference. The surgical treatment is radical or palliative. The writers state that an exploratory operation should be more frequently advised. They hold that results from the radical procedure in recent years are encouraging, and believe that the future should show a marked increase in the percentage of recoveries. In this connection they emphasize the great importance of an early diagnosis of the disease. The palliative surgical measures are undertaken to overcome the effects from stenosis of one or other of the cardiac orifices.

The monograph is concise and to the point. The statistics are of special value, as the cases were all observed under the same conditions. Careful studies of this kind do much towards increasing our knowledge of the diseases of particular organs.

A Text-book of the Practice of Medicine. By JAMES M. ANDERS, M. D., of Philadelphia. Fourth edition. (Philadelphia: W. B. Saunders & Co., 1900.)

Only a year has passed since the appearance of the third edition of this work, yet Dr. Anders has made many additions and recent literature has been frequently quoted in the present one. There are some things we miss, however. Little is said of the occurrence of typhoid bacilli in the urine of typhoid-fever patients. More emphasis might have been laid on the importance of thorough disinfection of the urine. Probably more cases of direct infection of typhoid have been due to the urine than to the faeces. In discussing the treatment of pneumonia, Dr. Anders advises the giving of large doses of strychnine hypodermically, as much as one-fifteenth of a grain every two or three hours. The administration of digitalis is only advised in the event of great cardiac weakness. The experience of this hospital has been that digitalis is of more service in these cases than the tincture of digitalis.

In reviewing a text-book of medicine there are certain sections that are probably most often first referred to as an index of the author's views. Of these, possibly that on appendicitis comes first. Dr. Anders here speaks with no uncertain voice. He considers that the physician and surgeon "should stand guard together from the moment the case is diagnosed or appendicitis is strongly suspected." The same remark might well be applied to many of the border-line conditions between medicine and surgery. He speaks for the vigorous use of salines in cases where there is peritonitis with pus-formation and operation cannot be performed.

The author still clings to elaborate tables of differential diagnosis throughout. The sections on diagnosis are good, but probably the best department is that of treatment. This is consistently good and a valuable feature of the work. There are few text-books in which this is better handled.

Atlas and Epitome of Special Pathologic Histology. Authorized translation from the German, by Doent Dr. HERMANN DURCK. Edited by LUDWIG HECTOR, M. D. With 62 colored plates. (Philadelphia: W. B. Saunders, 925 Walnut St., 1900.)

The first volume of this work deals with the pathological histology of the circulatory organs, respiratory organs and gastrointestinal tract. Two more volumes are to follow. The illus-

trations, which naturally occupy a considerable space in the atlas, are well printed on heavy paper, but the colors are disappointing. Several of the figures, however, are very good. The text is made up of short accounts of the various pathological processes. These descriptions, of course, do not pretend to be exhaustive, but the beginner in the study of pathology will no doubt find them very useful in connection with laboratory work. The book is not an attractive one at first glance, but its concise text and numerous illustrations make it a useful addition to a laboratory.

BOOKS RECEIVED.

Transactions of the Ophthalmologic and Otolaryngologic Association, at its Fifth Annual Session, held in St. Louis, Mo., April 5, 6 and 7, 1900.

Archives of the Roentgen Ray. Edited by Thomas Moore, F. R. C. S., and Ernest Payne, M. A. (Cantab). Vol. 5, No. 1, August, 1900. 4to. Rebman, Limited, London. Queen & Co., Philadelphia.

Cancer of the Stomach. A Clinical Study. By William Osler, M. D., and Thomas McCrae, M. B. (Tor.). With illustrations. 1900. 8vo. 157 pages. P. Blakiston's Son & Co., Philadelphia.

Transactions of the Texas State Medical Association. Thirty-second annual session, held at Waco, Texas, April 24 to 27, 1900. 8vo. 400 pages. Austin, Texas.

Tuberculosis: Its Nature, Prevention and Treatment. With special reference to the Open-air Treatment of Phthisis. By Alfred Hillier, B. A., M. D., C. M. With thirty-one illustrations and three colored plates. 1900. 12mo. 12 + 243 pages. Cassell & Co., Limited, London, Paris, New York and Melbourne.

Diseases of the Gall-bladder and Bile-ducts, including Gall-stones. By A. W. Mayo Robson, F. R. C. S. Assisted by Farquhar Maerae, M. B., C. M. (Glas.). Second edition. 1900. 8vo. 313 pages. Baillière, Tindall & Cox, London.

Transactions of the Indiana State Medical Society, 1900. Fifty-first annual session, held at Anderson, Indiana, May 24 and 25, 1900. 8vo. 478 pages. Indianapolis.

Essentials of Histology. By Louis Leroy, B. S., M. D. Arranged with Questions following each chapter. 72 illustrations. (Saunders' Question-Compends, No. 25). 1900. 12mo. 231 pages. W. B. Saunders & Co., Philadelphia and London.

Index Catalogue of the Library of the Surgeon-General's Office, United States Army. Authors and Subjects. Second Series, Vol. V. Enamel-Fyuner. 1900. 4to. 1127 pages. Government Printing Office, Washington.

Guy's Hospital Reports. Edited by E. C. Perry, M. A., M. D., and W. H. A. Jacobson, M. Ch. Vol. LIV, being Vol. XXXIX of the third series. 1900. 8vo. xli + 341 pages. J. & A. Churchill, London.

Modern Medicine. By Julius L. Salinger, M. D., and Frederick J. Kaltefleiter, M. D. Illustrated. 1900. 8vo. 801 pages. W. B. Saunders, Philadelphia and London.

Anomalies of Refraction and of the Muscles of the Eye. By Flavel B. Tiffany, A. M., M. D. Fourth edition. 1900. 8vo. 307 pages. Hudson-Kimberly Publishing Co., Kansas City, Mo.

Sexual Debility in Man. By Frederic R. Sturgis, M. D. 1900. 8vo. 432 pages. E. B. Treat & Co., New York.

Transactions of the Association of American Physicians. Fifteenth session, held at Washington, D. C., May 1, 2 and 3, 1900. Vol. XV. 8vo. xxi + 542 pages. Printed for the Association, Philadelphia.

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PRELIMINARY NOTE OF A CASE OF INFECTION WITH *BALANTIDIUM COLI* (STEIN).

BY RICHARD P. STRONG, M. D.,

Assistant Surgeon, U. S. A., Director of the Army Pathological Laboratory, Manila.

AND

W. E. MUSGRAVE, M. D.,

Hospital Steward, U. S. A., Resident Pathologist to the First Reserve Hospital.

(From the Army Pathological Laboratory, Manila, P. I.)

Balantidium coli (Stein), (*Paramecium coli*—Malmsten) was probably first observed by Lccuwenhoek. In a diarrhœa of considerable duration, he examined his own stools and recognized in them small motile animals, which, he stated, were about the size of red blood-corpuscles, and moved by means of small "fussartig" formations.

Leuckart intimated that the size of the parasite, as given by Lccuwenhoek, probably rested on a guess, as the latter author was not able to notice any flagella with the microscope of his time.

Malmsten,¹ in 1857, in Stockholm, first described the par-

asite in a patient who, for two years following a case of cholera, had suffered at first from digestive troubles and later from a painful diarrhœa. On examination of the patient he found, about an inch above the anus, a small wound, which excreted a thin, bloody pus. A great number of the parasites were constantly found in this discharge and also in the intestinal mucus and fœces. The condition of the patient improved considerably with the decrease in the number of the parasites. Lowen classified these parasites as belonging to the genus *Paramecium*.

In a second case Malmsten found the parasite in the bloody pus-like excretions of a woman suffering from a severe intestinal catarrh. The woman died. At necropsy, he states, the parasites were found on the healthy mucous membrane

¹ Malmsten: Infusorien als Intestinal-Thiere beim Menschen. Virchow's Archiv, Bd. xii, p. 302.

of the cæcum and in the vermiform appendix. They were, however, missing entirely in the small intestine. In small numbers they were found in the ulcers of the large intestine.

In 1862 Stein proposed the name *Balantidium coli* for the parasite.

In 1891 Mitter² was able to collect from the literature twenty-eight cases of infection with this parasite. Since this date, De la Chappelle³ (1896), has reported two other cases in man. The article of this latter author is not at hand.

Henschen especially emphasizes the pathological importance of this parasite, but other authors are inclined to the belief that its presence should only be considered as an accidental, unimportant complication. The latter view is the one which is generally expressed in our recent text-books regarding this parasite. Thus Opie⁴ (1900), in his article on Protozoa, concludes that *Balantidium coli* is apparently an accidental parasite which finds favorable conditions for growth in the diseased intestine and that it is improbable that the organism is the etiological factor in the production of the diarrhœa with which it is associated.

We wish to contribute another case to the literature of infection with this parasite.

The patient observed by us had lived in northern New England and came to the Philippine Islands in December, 1899. There was no history of previous diarrhœa. He stated that he had been perfectly well until April, 1900, when he began to have diarrhœa which continually grew worse. He entered the hospital here on June 9. From this date up to the time of his death, August 11, he had continuous, uncheckable, severe diarrhœa.

He became extremely emaciated before his death. During life, the blood-examination showed a relative increase in the number of the eosinophiles. The stools showed large numbers of flagellate infusoria measuring from 70μ to 110μ long by 60 to 72μ broad. The periphery is covered with fine actively motile cilia. At the anterior end is a funnel-shaped entrance which is surrounded by cilia and when the parasite is moving, gives the appearance of a

paddle-wheel revolving. An ectosarc and endosarc may be distinguished, and the parasite possesses the power to change its shape and may appear quite round. The endosarc contains a large somewhat kidney-shaped nucleus and two contractile vacuoles. The surface is lightly striated longitudinally. In the posterior end is an anus from which particles were observed, at times, to pass. The anterior end is more pointed than the posterior and more tapering. For some days before death, each drop of the patient's fæces, placed beneath a cover-glass, contained between 100 and 200 of these infusoria. The stools contained no other parasites, but mucus, blood and epithelial cells were present.

At necropsy, in the lower portion of the jejunum and ileum the mucosa was reddened and contained considerable mucus. In the large intestine the mucosa throughout was covered with bloody mucus which was easily washed off; beneath this layer the mucosa itself was very much reddened. There were a number of shallow ulcerations present in the mucosa whose edges were not undermined; their bases and margins had a blackish pigmented appearance.

Agar plate cultures from the heart, spleen, liver and kidneys were negative for organisms.

Sections of the large intestine stained in hæmatoxylin and eosin show *Balantidium coli* all through the mucosa and passing through the muscularis and submucosa; some of the sections show the parasites lying along the intermuscular septa of connective tissue and penetrating for a short distance between the muscular layers. There is an extensive eosinophilia in the mucosa, muscularis mucosa, submucosa and lymph follicles. The process seems more marked in the submucosa. The mucosa shows areas of necrosis and of hæmorrhage, with cellular infiltrations and desquamation of cells. In the submucosa there are also infiltrations of round cells; the vessels are injected and often about the veins which contain the parasites small hæmorrhages have occurred. The lymph follicles are swollen. The liver shows small areas composed of round cells.

We cannot regard this parasite as a harmless one, for we could not explain the persistent diarrhœa of our patient without regarding it as the exciting cause, nor were we, from the lesions found at necropsy, enabled to explain his death in another way. A complete report of this case will appear shortly.

OCTOBER 4, 1900.

² Mitter: Beitrag zur Kenntniss des Balant. coli. Inaug. Diss., Kiel 1891.

³ De la Chappelle: Finska läk.-sällsk. handl., Helsingfors, 1896; xxxviii, 1041.

⁴ Opie: Twentieth Century Practise of Medicine, vol. xix, 1900.

HYPEREXTENSION AS AN ESSENTIAL IN THE CORRECTION OF THE DEFORMITY OF POTT'S DISEASE, WITH THE PRESENTATION OF ORIGINAL METHODS.¹

BY R. TUNSTALL TAYLOR, B. A., M. D.,

Surgeon to the Hospital for Crippled Children, Baltimore; Fellow of the American Orthopedic Association, etc.

Any successful treatment of tubercular spondylitis must be based on a careful consideration of the anatomical, patho-

logical and mechanical problems involved, and any method determined on must stand the test of clinical experience before acceptance.

Let us first consider briefly some of the chief anatomical features of the spine from the standpoint of the mechanics

¹ Read, in part, at the Fourteenth Annual Meeting of the American Orthopedic Association, on May 2, 1900, Washington, D. C.

in the causation and in the treatment of this tubercular osteitis of the vertebrae.

The vertebral column as a whole consists of four curves when viewed laterally—a convexity forward in the cervical region, a convexity backward in the dorsal region, a convexity again forward in the lumbar region and backward in the sacral.

The three first-mentioned curves, with which we are only concerned, are subject to variations dependent on whether the individual is standing or sitting, and also whether the observation is made on rising in the morning or late in the evening, being in the latter cases more marked.

It has been shown by Brackett² that recumbency in a prone position lessens these curves, and supine recumbency has been used from time immemorial as an efficient means of treating spinal curvatures.

Suspension by the head and hands also renders these physiological curves, if we may so designate them, less appreciable. Le Vacher³ demonstrated this in 1768 in his "L'arbor suspendens" attached to a corset.

The "jury-mast," for which Lee⁴ gives the credit to J. K. Mitchell in 1826, and Lee's own "self-suspension spinal swing," devised in 1866, confirmed this observation. We know now, however, that these physiological curves are chiefly lessened by suspension and not the curves due to tubercular disease as the earlier observers thought.

In the erect posture the spine must bear the superincumbent weight of the head, and by means of the ribs and diaphragm also the weight of the thoracic viscera, and, to a certain extent, the liver and other abdominal organs. Further, through the sternal attachments of the shoulder girdle and the anterior situation of the arms, there is to a certain extent also, a drag downward and forward on the dorsal spine by them.

If the spine, as a whole, is viewed in profile in either a skeleton or a fresh specimen, it will be seen that a vertical line drawn through the bodies of the cervical vertebrae will pass anterior to the dorsal vertebrae, not touching them, but in the lumbar region such a line will again reach the vertebral bodies. Thus, from an anatomical standpoint, we may conclude that the mechanics of the spinal column decidedly predispose to a *dorsal* convexity, or kyphosis, even without the addition of disease, which the continuity of the vertebral bodies and intervertebral fibrocartilages antagonize anteriorly, and the ligamenta flava, inter- and supraspinalia posteriorly.

Secondly.—From the pathological findings in caries of the vertebrae, since the time of Sir Percival Pott (1779), observers have noted that the less compact bodies of the vertebrae are the seat of the tubercular osteitis, softening and disintegration and not the denser articular and transverse processes, as a rule. As a result of this in untreated, maltreated and neglected cases, the characteristic deformity

has occurred, *i. e.*, the superior and inferior edges of the bodies of the involved vertebrae have come into closer contact anteriorly and the spinous processes are more widely separated than is normal (Fig. 1). In addition, unless means are adopted to check this, the healthy vertebral bodies will come into contact with those diseased, and from the traumatic irritation produced thereby and the contiguity, the healthy vertebrae will also become involved in the process and so the diseased area will extend.

What, then, can we gather from this, as the indication for the treatment to combat this normal and pathological tendency to kyphosis? Manifestly it is the maintenance of hyperextension of the spine until all danger of extension of the tubercular process is passed and firm cicatrization has occurred from the layer of non-tubercular granulation tissue, which is converted in time into fibrous tissue, cartilage or bone and locks the vertebral bodies or processes together inseparably by ankylosis.

I have illustrated this diagrammatically (Fig. 2): Let Fig. 2A represent two healthy vertebrae seen in profile. The parallel lines represent the superior and inferior planes of those bodies. The centre of gravity or weight-bearing line is indicated by the dotted line, seen to pass through the centre of the vertebral bodies. The alignment of the spinous processes is seen to be straight.

In Fig. 2B we see the result of an untreated tubercular process where the bodies have collapsed, the planes of the superior and inferior surfaces converge and meet anterior to the vertebral column and the spinous processes are widely separated. The centre of gravity line is thrown further forward, tending to increase the deformity. The separation of the spinous processes shows the characteristic contour of the hump-back.

In Fig. 2C is shown what should be the aim of treatment; the separation of the vertebral bodies as far as the ligamentous and muscular attachments will permit; the throwing of the centre of gravity back on the articular processes and the crowding together of the spinous processes. We cannot say that a true separation of the vertebral bodies really occurs by hyperextension before extensive bone destruction has taken place, but certainly intravertebral pressure is lessened on the bodies thereby. On the other hand, Bradford and Cotton's⁵ experiments lead us to suppose in extensive unhealed disease such a separation certainly occurs in hyperextension.

To meet this aim of treatment, in the latter part of 1894 I presented before the Johns Hopkins Medical Society⁶ what I termed an apparatus for applying plaster jackets on the plaster jacket stool on which the patient sat, with the pelvis fixed, the arms extended upwards and backwards, and traction was made on the head by means of a head-sling. The result of this attitude on the spine was lordosis. In that paper, as far as I can find out in the literature, I first called

² Bradford and Lovett, *Orthopedic Surgery*, 2d edition, 1899, 53.

³ *Memoirs de l'Académie royale de chirurgie*, Paris, 1768, tome (4).

⁴ *Transactions American Orthopedic Assoc.*, vol. iv, 244.

⁵ *Boston Med. and Surg. Jour.*, Sept. 20, 1900, 279-280.

⁶ *Johns Hopkins Bulletin*, No. 45, February, 1895, and *Medical News*, March 23, 1895.

attention to and demonstrated clinically the importance of extending the spine backwards (hyperextension) and the maintenance of this position by means of plaster of Paris jackets for the prevention or correction of the natural tendency of the deformity of Pott's Disease (Fig. 3). However, Hadra in 1891 suggested the same principle by wiring the spinous processes together, "thereby relieving the vertebral bodies," but in the article it is stated he has not done this operation in Pott's Disease.⁷ Other methods to accomplish the same end were published by other observers shortly after.

Chipault published on March 9, 1895, his method of wiring the spinous and transverse processes in Pott's Disease after "forcible correction" of the deformity under anæsthesia by manual traction on the head and extremities and pressure on the gibbosity.⁸

Calot published a paper on similar operations in 1896.⁹

Goldthwait reported, in 1898, his and Metzger's excellent method of hyperextension, without anæsthesia, in which the patient lies supine on two strips of steel, that portion of the spine above the knuckle being unsupported and gravity acting as the correcting force.¹⁰

Redard in the same year published his method of mechanical traction in a prone position with anæsthesia and manual pressure on the boss.¹¹

In 1899 I presented to the American Orthopedic Association¹² my plaster jacket stool, supplemented with a pressure rod (Fig. 4), to control the point at which hyperextension was to be made (viz., at the kyphosis) and called the apparatus "The Kyphotone" (*κυφός*, hunchback, and *τείνειν*, to extend). I found that without pressure on the knuckle in mid-dorsal cases, the lordosis, or hyperextension, frequently was more marked in the lumbar region than in the region of disease and more marked than was desirable, but the pressure rod on the knuckle obviated this, making the region of the gibbosity the centre of this arc (Figs. 5, 6 and 7).

The comparative value of suspension and hyperextension in the correction of the deformity of Pott's Disease is well shown in the photographs (Figs. 8 and 9). In Fig. 8 (a double photographic exposure) the lower photograph shows the child sitting on the kyphotone and the knuckle is well seen against the background. The upper photograph shows the child suspended by the Sayre head-sling and the knuckle is virtually of the same size it was before traction was made. In Fig. 9 we see traction has been made on the head, the arms have been carried upwards and backwards, the pelvis has been made fast and the pressure-rod has been applied, causing hyperextension at the knuckle, with the result that the spine is virtually straight.

This year I wish to present two recumbent kyphotones which carry out the same mechanical principles of hyperextension.

The larger is similar in many details to the one attached to the office stool, but differs in having the patient lie in a supine position on a plate or pelvic crutch instead of sitting up. The main bar slides in a solid metal block and thus can be lengthened or shortened to adapt itself to the patient's size.

The pressure-rod, attachments for hands and head-sling are similar to the upright kyphotone (Figs. 10 and 11).

The smaller kyphotone is quite simple, inexpensive and can be easily taken apart and carried in a satchel to a patient's house. It consists of two solid bases and uprights, one surmounted by a plate of sufficient size to support the pelvis and the second by a small plate to press upwards against the knuckle. This latter plate is adjustable and can be raised or lowered to increase the pressure and vice versa. The distance between the uprights can also be regulated by a rod attached to the bases by set-screws. The plate of the pressure-rod is incorporated in the plaster jacket during its application, but can be easily slipped out after the patient is removed from the machine by making an incision on one side of the pressure-rod in the plaster, which at this stage has not entirely hardened (McKim's modification). Then the opening thus made can be entirely and easily closed by moulding together the moist edges (Figs. 12 and 13).

Both of these recumbent kyphotones have been made to meet the need of acute or early cases or those with external pachymeningitis with paraplegic symptoms, in which it is detrimental to even sit up momentarily until the head-sling is adjusted and the superincumbent weight removed.

I have made an additional use of the larger recumbent kyphotone, and had attachments made for the mechanical correction of scoliosis of a severe and advanced grade, and I have used it also as a twisting correction machine daily on such cases or to obtain a corrected position in which it is deemed advisable to hold the patient constantly by means of a plaster jacket. Lovett has of late shown the value of hyperextension in the treatment of scoliosis,¹³ but the scope of this paper will not permit of further mention of this use of the recumbent kyphotone (Figs. 14, 15 and 16).

The question of which of these machines we shall use to prevent, correct or improve the deformity of Pott's Disease depends on the pathological condition we find the spine in, as shown by its flexibility, the size of the knuckle not necessarily being a determining factor of the latter.

(1) *Earliest Stages*.—At this period there is no deformity to correct, but the child will indicate by its posture, carriage or gait, grunting respiration, pain, night cries, muscular spasm or some of the characteristic symptoms, that spinal trouble is present. The region can be located by an expert and prevention of deformity obtained by plaster jackets applied in slight hyperextension on the small recumbent kyphotone.

⁷ Hadra, Trans. Amer. Ortho. Assoc., vol. iv, 205.

⁸ Chipault, *Medicine Moderne*, No. 20, Sixieme Année.

⁹ Calot, Trans. Acad. Méd., Paris, 1896.

¹⁰ Goldthwait, Trans. Amer. Ortho. Assoc., vol. ix, 1889; Boston Med. and Surg. Jour., July 28, 1898.

¹¹ Redard, *Archivio di Orthopedia*, 1898, Fasc. 2.

¹² Transactions, vol. xii, and N. Y. Med. Jour., May 12, 1900, 716.

¹³ Boston Med. and Surg. Jour., June 14, 1900.

At this stage caseation and conglomeration of the tubercles is beginning and traumatic contact from pressure of the healthy adjacent vertebræ is ripe to help break down the diseased vertebral body.

Unfortunately, the orthopedic surgeon rarely has an opportunity to try his skill at preventive medicine, as the general practitioner and general surgeon, for that matter, either retain the ease themselves, using antiquated methods and recall hazily *one* lecture at college on "spinal disease," in which same "orthopedic lecture" nine times out of ten are given scoliosis, club-foot, flat-foot, bow-legs and all the rest, as well as "anteroposterior curvature." Or else the treatment (?) is referred to that paragon, the blacksmith—instrument-maker and pathologist.

(2) *Beginning Deformity.*—Thanks to the above treatment (?) or to the fact that the general practitioner *et al.* has been so busily engaged in diagnosing the thoracic or abdominal pain he has failed to strip and roll the child over and look at its back, the knuckle is discovered by the child's mother. In such a case the vertebral body has partially broken down and abscess-formation has begun. Correction may be obtained by gravity with the small recumbent kyphotone and maintained by a plaster jacket.

(3) *More Advanced Cases.*—In a case in which several vertebral bodies have broken down, and in which some adhesions or fibrous ankylosis are just starting to form, either the large recumbent or upright kyphotone may be necessary to correct, with head-sling traction and pelvic fixation. It is at times astonishing to see a large hump disappear under this treatment (Figs. 8 and 9).

(4) *Neglected or Ankylosed Cases.*—If the ankylosis in a case is solid and condensing osteitis has taken place, *no extreme force is justifiable*. Pain should be the guide to the amount of pressure or traction force used. Even, however, in large knuckles or humps, it may be found the ankylosis is not solid, and it is certainly justifiable to lessen the deformity of such a case by one of the more powerful kyphotones and allow the spine to heal in an improved position.

The method suggested by Bradford and Vose¹⁴ would seem also applicable to the first two of the foregoing varieties. This method consists of allowing the child to lie on its back and be slung in a position of hyperextension by a piece of firm cloth passing under the kyphos. This cloth, after passing around the side, is attached to a pulley, by means of which the hyperextension of the spine can be regulated.

When we consider the three regions of the spine to which hyperextension in Pott's Disease may be applied, we find difficulties confront us in each. In the cervical region with its normal lordosis the application of plaster of Paris bandages presents difficulties both as to efficiency, comfort and the avoidance of a bungling mass around the neck. A child's neck is so short, and with a traction head-sling on, it is next

to impossible to apply an efficient bandage. The best plan is to use a steel back-brace with a head-support, but this will not correct the deformity. Instead of the head-support, or in conjunction with it, I have of late used a steel back-brace extending upward to or just above the kyphos and at this point had two buckles attached for a padded webbing strap to pass around the front of the throat. By tightening this strap the falling forward of the cervical segment can be limited or lessened, and it is astonishing how tight this strap can be borne. At first the patient gets quite livid in the face, but in a day or two the circulation adapts itself to the new condition and the child involuntarily holds the neck back, away from the strap, by means of the posterior muscles. I have seen no embarrassment of respiration and the superincumbent weight of the head is transferred to the healthy articular, transverse and spinous processes.

From the sixth (6) dorsal vertebra upward, our dependence must be placed on the steel back-brace with supplementary straps to hold the shoulders and neck well backwards. From this point downwards the plaster jacket can be used, applied in hyperextension, but owing to the normal kyphosis, extreme hyperextension is difficult and *entire* correction of a severe deformity is rarely possible, except in very early cases. In the lumbar region, where normal lordosis already exists, it is easy to overdo the hyperextension with the result that the patient has a pot-bellied or sway-backed appearance. This can be avoided by making the head traction upward and slightly forward (not upward and backward); or, by a modification one of my assistants, Compton Riely, has made, to exert pressure against the anterior superior spines in front and behind the trochanters major to prevent tilting forward of the pelvis, he having noticed in the majority of cases that the chief part of the lordosis was pelvic (Fig. 17).

Another method of obviating this excess of lordosis is to flex the thighs on the body, thereby relaxing the psoas pull on the lumbar spine and preventing the rotation forward of the pelvis.

I have not attempted the use of anæsthesia with these methods of applying correction to Pott's Disease, but rather avoided it as unnecessary and dangerous. The pain caused is inconsiderable in reduction and the resulting jacket is a relief to the painful symptoms previously present. These methods permit of the application of mechanically correct jackets, *i. e.*, those in which firm, even pressure is exerted against the three important points; the kyphos behind, the whole length of the sternum and ribs and the anterior spines of the ilia in front.

As I have said, in spines in which I suspect ankylosis I do not use great force, simply rendering them as straight as possible, *short of pain*. So-called "forcible correction," by which is meant manual traction and pressure under an anæsthetic, has but few adherents here in America, the majority of us feeling loath to tear by great force structures we could not appreciate on account of the anæsthetic, pain

¹⁴ Annals of Surgery, 1899, vol. xvii, 223.

being eliminated. Fatal and untoward results have been reported by Sherman,¹⁵ Jonnesco,¹⁶ Lorenz¹⁷ and others.

The tracings (Fig. 18) show the results in a few cases of the Hospital for Crippled Children. The stated duration of the disease is indicated under the initials of the case and it can be easily seen how much better results, as a rule, are obtained ultimately in cases treated early. On the other hand, when the size of the gibbosity is considered, quite an unexpected and appreciable improvement is shown in some of the cases.

As to the comparative value of the three machines, the upright kyphotone finds more general application than the

For conclusions as to these methods of correcting the deformity of Pott's Disease and applying plaster jackets, I would say:

First. The jackets thus applied fix the spine in the most advantageous position for lessening the tendency for the production of deformity.

Second. The rapidity and ease with which jackets may be applied.

Third. These methods are applicable to mid- and lower-dorsal and lumbar caries. Above the sixth (6) dorsal, a steel back-brace with head-support or throat-strap must be used.

Fourth. It seems comfortable to the patient, as the

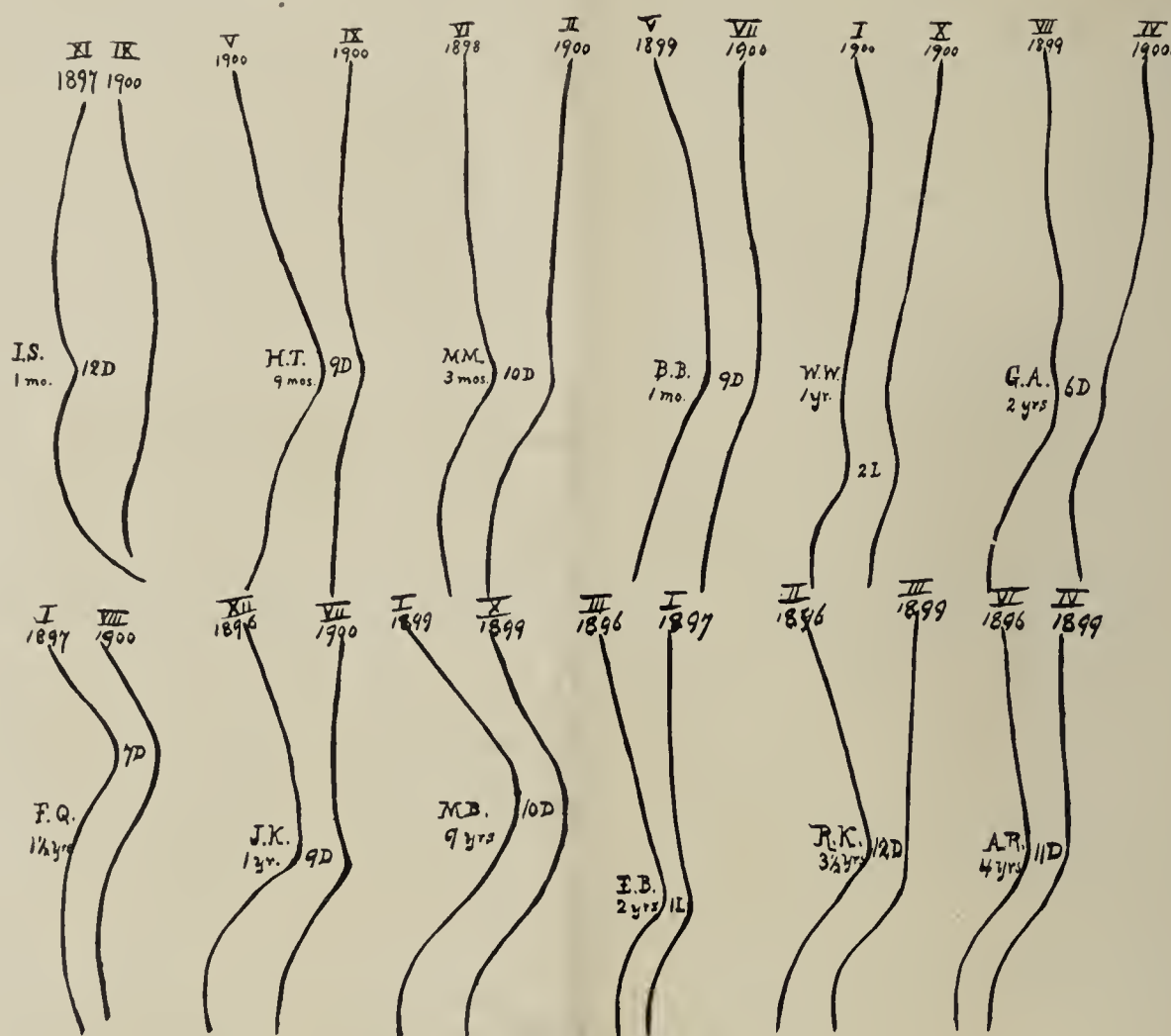


FIG. 18.—Tracings from (12) out-patients treated by kyphotones. Above each line is the date; to the left are the initials of the case and the duration when first seen. Between each pair of lines is given the vertebra chiefly involved.

other two, as in the stage in which the majority of cases present themselves the knuckle is somewhat advanced in formation and slight adhesions exist; further, the patient can be viewed from all sides and the ultimate appearance of the jacket is at all times apparent. It is the quickest method, all things considered.

For the early stages the small kyphotone acts admirably, and for cases with paraplegia or acute symptoms with an advanced kyphosis, the large recumbent kyphotone is needed.

thorax is well supported and the superincumbent weight is removed from the diseased vertebral bodies to the healthy articular processes. Quite an appreciable gain has been noticed in the nutrition of patients after this method is used, due largely to the increased lung-expansion, which the posture renders possible.

Fifth. Absolute immobilization of the patient in the desired corrected position is obtained, one person being able to apply the methods without assistants to steady the patients, as nothing can slip at the most important moment.

Sixth. Hyperextension has been used constantly in the Hospital for Crippled Children in applying jackets on all suitable cases, from 1895 to the present time, and its efficacy has been demonstrated to our satisfaction clinically.

¹⁵ Pacific Record of Med. and Surg., October 15, 1898, 73.

¹⁶ Communication to Twelfth Internat. Congress of Med.

¹⁷ Deutsch med. Wochen., 1897, 556.

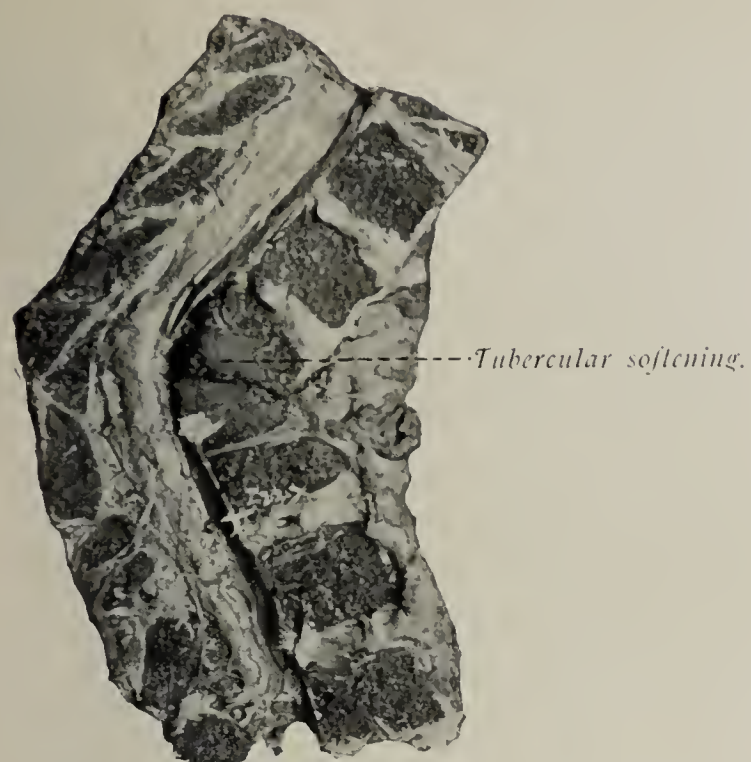


FIG. 1.—Spine. Lower Dorsal Region. Child. Vertical antero-posterior section. One intervertebral disk destroyed and the anterior adjacent edges of vertebral bodies softened and disintegrated. Extension of the process backward to dura, and forward among prevertebral ligaments. Moderate knuckle. (Nichols).

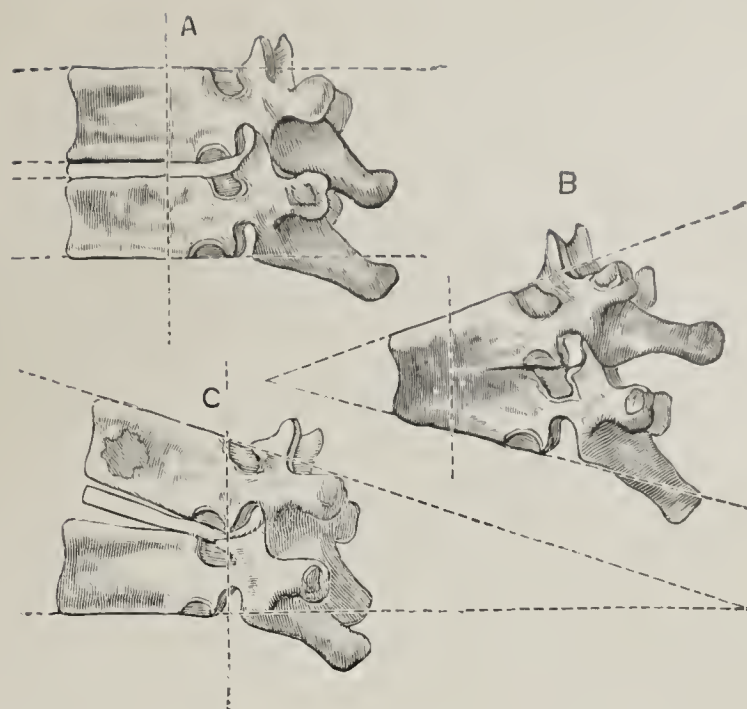


FIG. 2.—Diagram showing (A) Normal position of adjacent vertebræ. (B) Falling forward of the vertebral bodies in caries of the spine. (C) The aim of treatment of Pott's Disease by means of spinal extension in its true sense.

— — — — — The planes of the vertebral bodies.
 - - - - - The line of the centre of gravity and of the superincumbent weight.



FIG. 3.—The original plaster jacket stool. 1895.

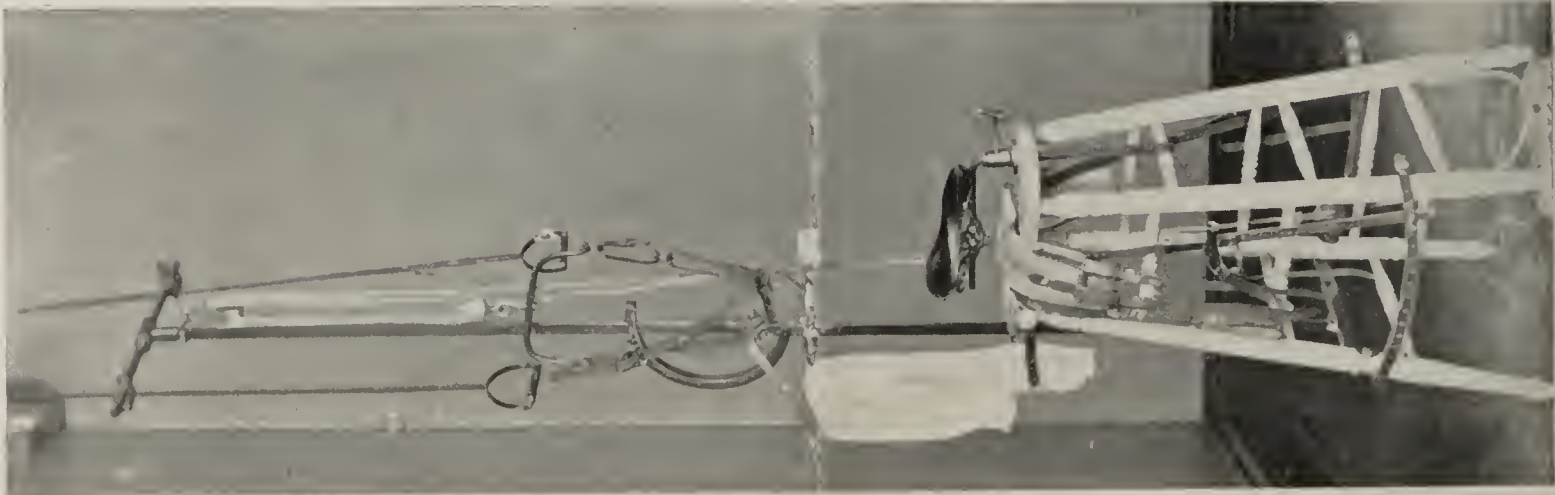


FIG. 4.—The kyphotone.

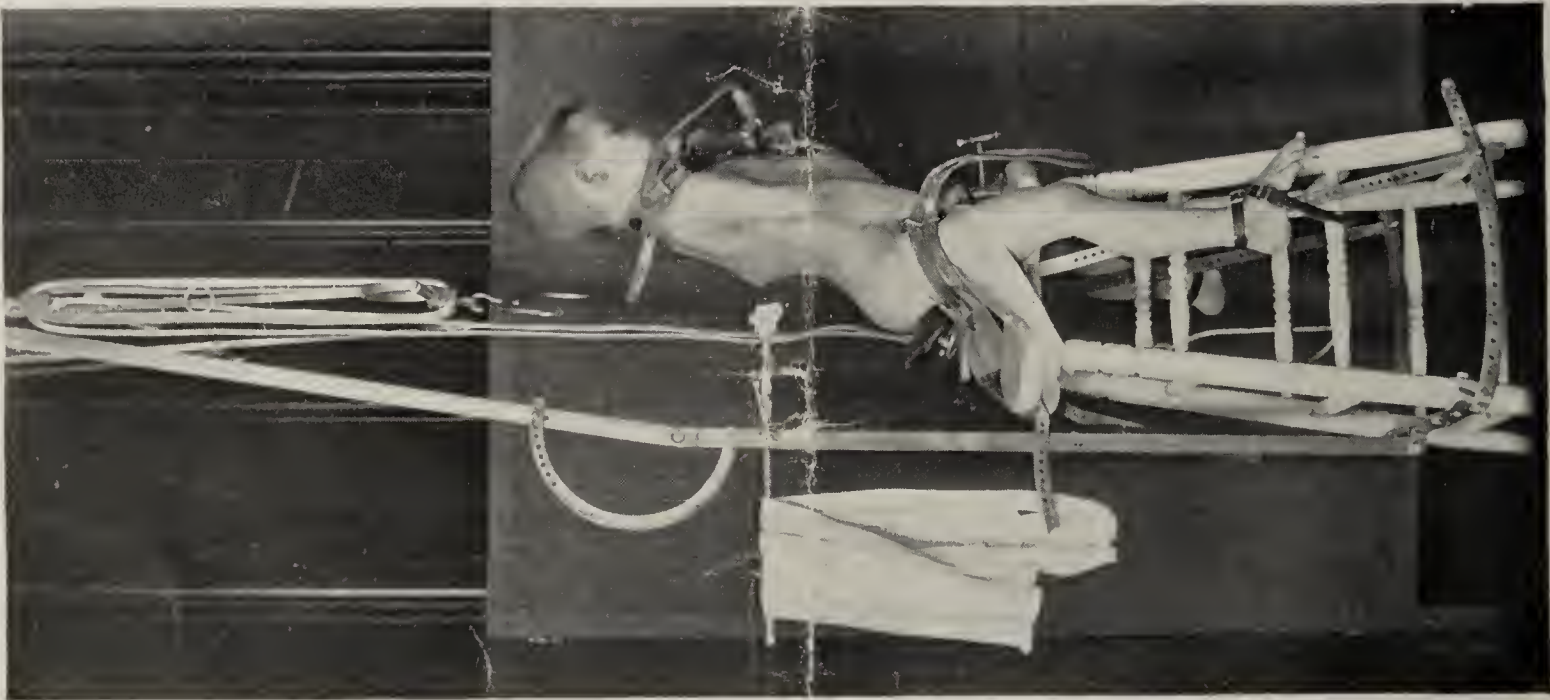


FIG. 5.—A patient (J. K.) on the kyphotone before reduction.

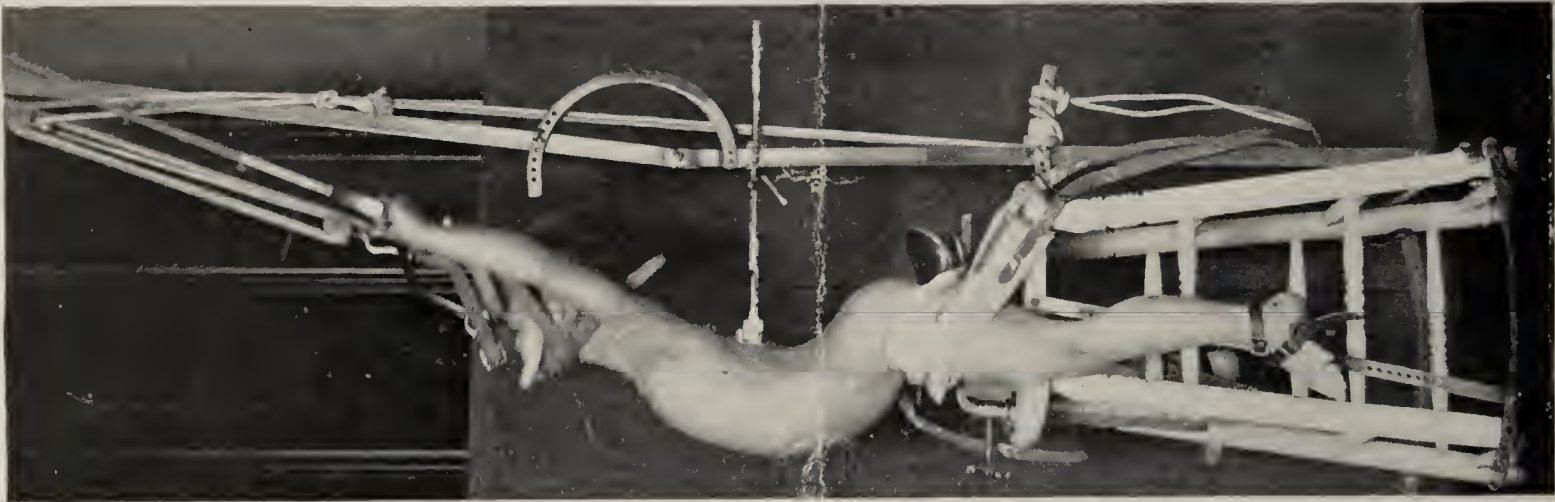


FIG. 6.—A patient (J. K.) on the kyphotone during the reduction of the kyphos.

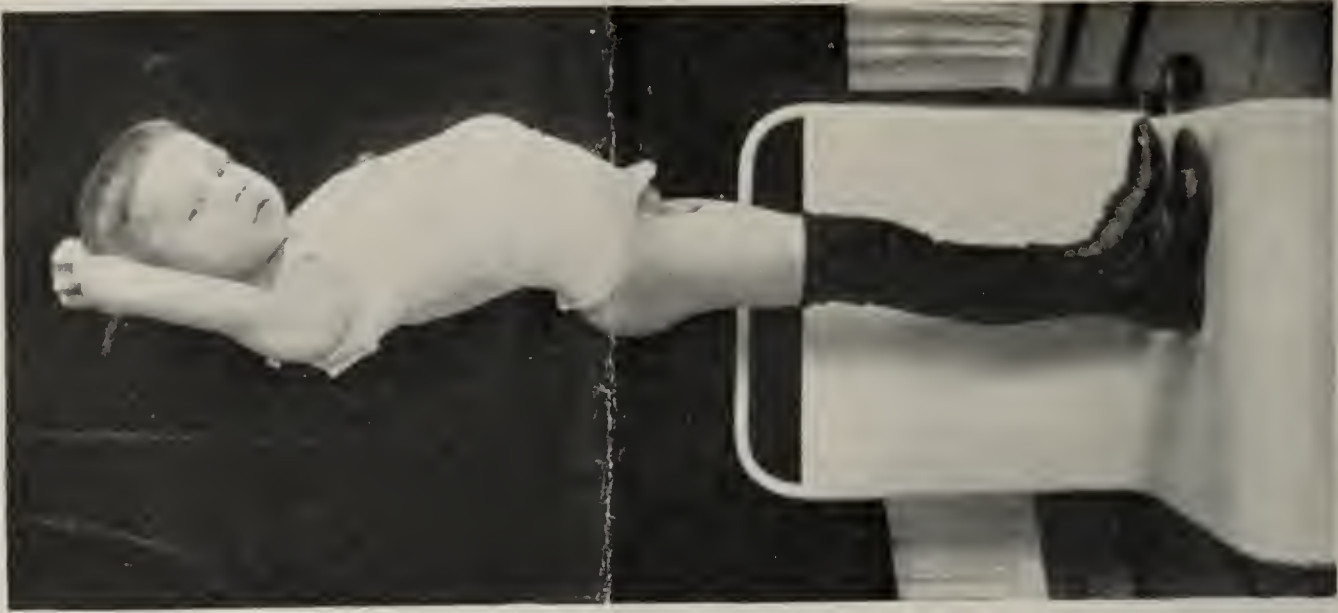


FIG. 7.—A patient (J. K.) showing the result of reduction.



FIG. 8.—A double photographic exposure.
Lower figure shows child (H. T.) in sitting posture.
Upper figure shows child (H. T.) suspended by head, with no reduction in the kyphosis.



FIG. 9.—Shows child (H. T.) hyperextended with obliteration of the kyphosis.

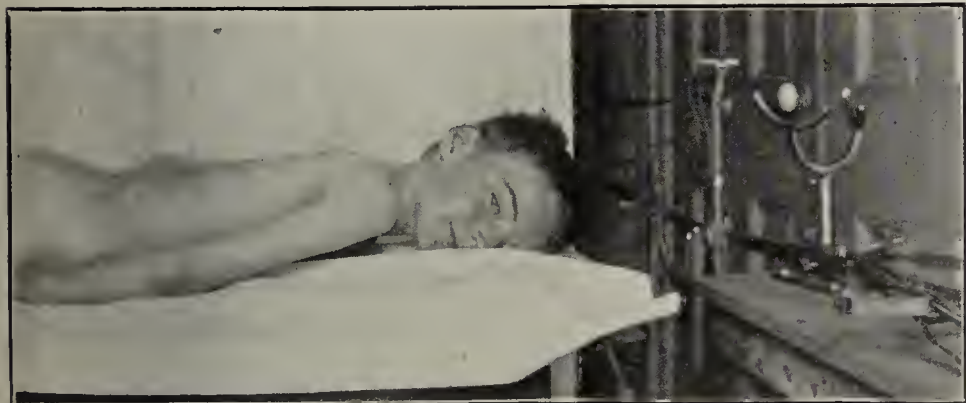


FIG. 10.—Case (W. W.) showing deformity. Kyphotone seen on the right.

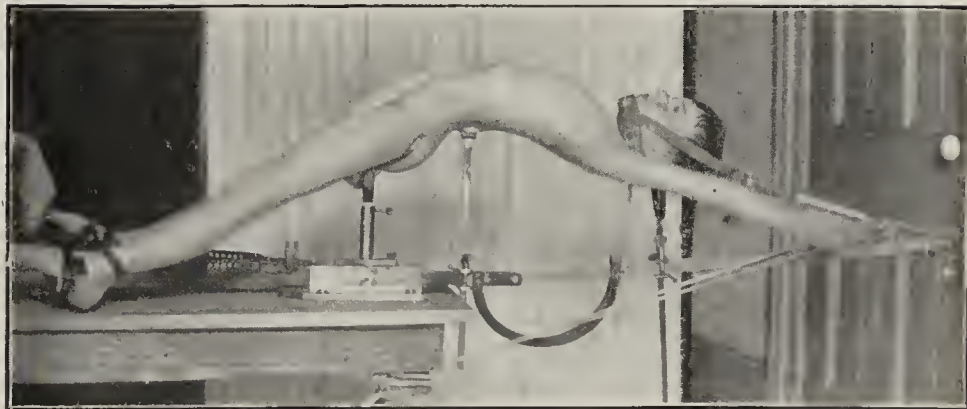


FIG. 11.—Case (W. W.) seen on the large recumbent kyphotone.



FIG. 12.—Case (B. B.) and small recumbent kyphotone.



FIG. 13.—Case (B. B.) showing complete obliteration of the deformity.



FIG. 14.—Case (C. N.) scoliotic.



FIG. 16.—Case (C. N.) showing correction effected on large recumbent kyphotone and maintained by a plaster jacket.

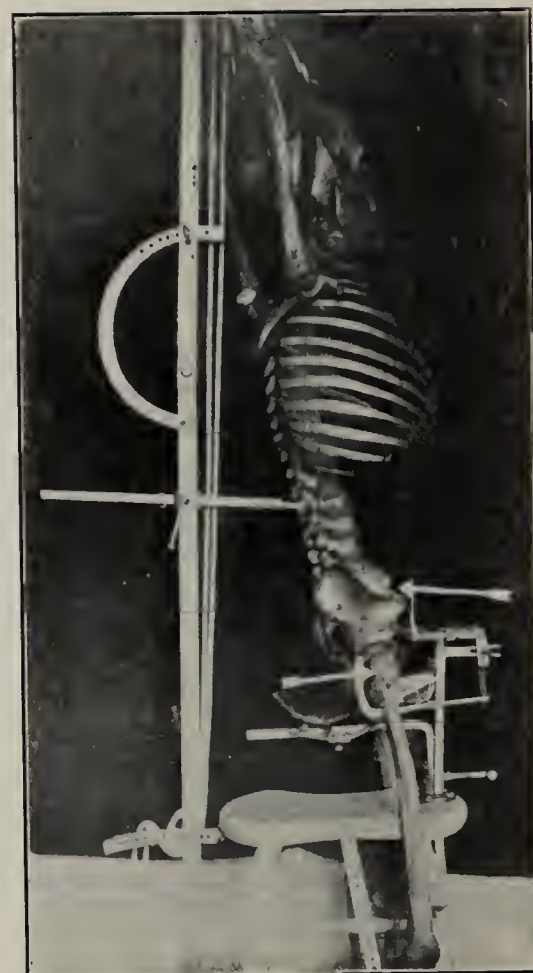


FIG. 17.—Compton Riely's modification, adjustable by set-screws to any pelvis. Arrows indicate points where pressure is made.

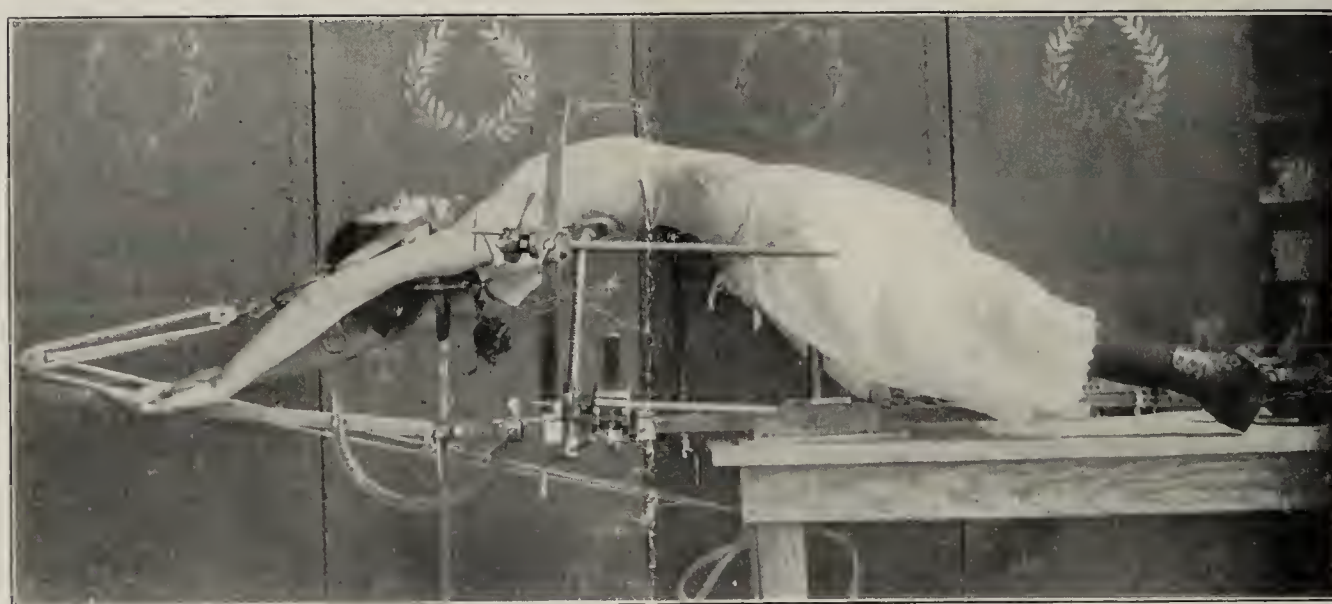


FIG. 15.—Case (C. N.) on large recumbent kyphotone.

Seventh. Aside from the danger of excessive and unequal force being used manually by *several* persons making traction for "forcible correction" under an anæsthetic, these methods enable *one* operator to adjust to a nicety his pressure and traction without an anæsthetic and further enable him to make his diagnosis as to the pathological stage the process has reached, which the size of the deformity does not always tell, in regard to the degree of ankylosis.

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TWO EXAMPLES OF BENICE JONES' ALBUMOSURIA ASSOCIATED WITH MULTIPLE MYELOMA.¹

A PRELIMINARY REPORT.

BY LOUIS P. HAMBURGER, M. D.,

Assistant in Medicine, Johns Hopkins University.

On the 13th of last month, Dr. Iglehart brought me a specimen of urine with the remark that it contained an

albuminous body having peculiar properties. It had been voided by one of his patients in large quantity—about 3,500 cc.—in the twenty-four hours. We examined it and found that it afforded the reactions which I shall demonstrate to you to-night.

¹ Demonstration before the Johns Hopkins Hospital Medical Society, November 5, 1900.

As you see, it is very pale, of an acid reaction, with a specific gravity of 1,004. It gives a white ring when floated over nitric acid. Heated to a temperature of about 55° , a heavy milk-white precipitate appears. Boiled, the fluid becomes clearer, only to become more turbid on cooling. The addition of acetic acid to the fluid after reaching its maximum turbidity causes it to become clear again. A few drops of nitric acid yield a precipitate which dissolves completely on boiling and reappears on cooling. In the Esbach albuminometer the proteid content reaches 0.27 per cent. The urine gives a strong biuret reaction. Let it be added that no casts were seen even in a centrifugalized specimen.

We recognized that this condition was no ordinary albuminuria. It is not the usual urine of nephritis, although the positive Heller's test alone might lead one astray. But the usual albumins of albuminuria, after being precipitated by heat, are not dissolved by the addition of a small quantity of acetic acid; they do not tend to redissolve on boiling; the nitric acid precipitate does not dissolve on boiling and reappear on cooling and the biuret reaction is wanting. The substances which do offer these reactions are the albumoses; the condition is that of albumosuria, and so I designate it in the present instance.

From an acquaintance with the literature on the subject, I was able to point out to Dr. Iglehart that this condition of so-called albumosuria in such a marked degree was an accompaniment of sarcomatosis of the bone, and, indeed, of a peculiar variety originating in the marrow and known as myelomata, new growths affecting for the most part the skeleton of the trunk—the vertebræ, the clavicles, the sternum and the ribs. Whereupon he recalled that his patient had had on two occasions most intense pain in the ribs and had lost much weight during the past three months.

So convinced was he by the data which were presented to him, that he gave a member of the family the serious prognosis which the condition merits.

Dr. Iglehart has given me further details of this peculiar illness. He was called to see the patient, a lady 49 years of age, in August, 1900. Previously healthy, she was suddenly seized at this time with sharp pain over the 9th left rib near its cartilaginous attachment. The pain was severe and increased on deep inspiration. There was tenderness on pressure over the painful point. Neither crepitus nor a friction rub was present. The condition so resembled a fracture that he considered the patient had injured the rib, but he could elicit no history of trauma. Within three weeks the pain had disappeared. She was again seen in September, this time complaining of nausea without apparent cause. Her general health had suffered; she had lost thirteen pounds in weight.

Early in October she was seized a second time with pain, now in the region of the 8th right rib in the mid-axillary line. It was at this time that the remarkable urinary condition was discovered. The patient herself had noted that since the past summer she had drunk more water than usual and had voided a larger quantity of urine.

Dr. Osler saw the patient on November 3d, two days ago, and aside from a slight pallor of the visible mucous membranes, the physical examination was negative.

In short, however absurd it may seem at first thought, from examinations of the urine I was confident I had established the probable diagnosis of new growth of the bonemarrow.

Excepting in diseases of the urinary tract itself, I know of only one other instance in which, without having seen the patient, the diseased organ may with great probability be determined from an examination of the urine. I refer to the presence of leucin and tyrosin in the urine as a sign of widespread destruction of liver substance.

Following the recognition of this example of albumosuria with its consequent diagnosis, Dr. Osler called my attention to the patient who lies before you, and it is to his courtesy that I am indebted for the privilege of reporting an abstract of her history.

The patient is a colored woman 50 years of age, who entered the medical clinic of the Johns Hopkins Hospital October 10, 1900, complaining of "rheumatism" and a "sprained hip." Regarding her family history she can only recall definitely that her father died of old age; that her mother, eight brothers and a sister have died from causes unknown to her; and that a sister is living and well.

She suffered the diseases of childhood and twenty-four years ago had "rheumatism" in both knees. Ten years ago she contracted grippe, and since then has had a cough each winter.

For about a year she has had pain in the region of the right groin and hip. One night last June, while picking up a bucket of coal, she experienced a remarkable sense of lengthening in the left arm and the next morning found that she could not raise it to her head because of pain and a feeling of weight. A week later the right arm became affected. She had pain here as well as in the shoulder, back of neck and chest. About this time the patient noticed a swelling the size of a hen's egg on the back of her head. Pain and stiffness in the arms continued so that by August she could neither cut her food nor feed herself. Six days before admission to the hospital, while walking, the right leg "gave away" without apparent cause. She fell to the ground, and since then has not been able to stand or walk. She has suffered great pain in the right hip. The patient has lost much weight and strength during her illness.

As you see, she is markedly emaciated. The mucous membranes are pale. Any movement of the body calls forth great pain. Over the occipital region there is a round, soft, fluctuating mass about 10 cm. in diameter, not adherent to the skin, not movable on the deeper tissues, not tender. A nodule three to four cm. in diameter is visible on either clavicle over its inner third. The one on the left is a little larger and more definitely circumscribed. It has evidently eroded the bone, for manipulation causes pain and crepitus. There is another tumor in the left supraspinous region about 4 cm. in diameter and evidently connected with the

acromion process of the scapula. The right lower limb is rotated outward and is abducted. The upper third of the thigh on this side is markedly enlarged and deformed by the presence of a tumor, about the size of a child's head, projecting from its postero-external aspect. It is firm and tender on pressure. An attempt to move the limb causes intense pain.

The lungs are clear on percussion. Here and there an occasional crackling râle is heard with inspiration. The point of the heart's maximum impulse is visible in the fourth left interspace 7 cm. from the midsternal line. A systolic murmur is audible at both the mitral and pulmonary areas. The abdomen is distended and held rigidly. No masses are to be felt. Neither the edge of the liver nor the spleen is palpable. There is no general glandular enlargement. The red blood-corpuscles number 3,548,000; the leucocytes, 4,500; hæmoglobin, 52 per cent. The relation of the different varieties of white corpuscles is practically normal.

Now, here is a case in which the clinical picture is clearly one of sarcomatosis of the bone. Does the urine exhibit the characteristics of albumosuria? As a matter of fact it does.

The urine is turbid, light yellow, and 600 to 800 cc. are voided daily. It is usually alkaline, though at times neutral in reaction. Its specific gravity varies from 1.012 to 1.030. Heller's reaction is positive. Acidified and heated to a temperature of 56° C., a heavy white precipitate appears. It redissolves in part on boiling and returns on cooling. The nitric acid precipitate disappears on boiling to reappear on cooling. The mixture assumes a darker color and particles of the precipitate adhering to the tube become pink. The biuret reaction is marked. The proteid content measured by the Esbach albuminometer varies from 0.3 to 0.6 per cent. Finally, Dr. Dorothy Reed has, by saturating the urine with ammonium sulphate and redissolving the precipitate, demonstrated more precisely the albuminose nature of this urinary constituent.

Some hyaline casts are present in the sediment.

This second case needs no peculiar explanation, but our diagnosis of neoplasm of the bone from examinations of the urine of Dr. Iglehart's patient needs justification.

The occurrence in the urine of proteids other than serum albumin is an old observation. Almost thirty-five years ago Lehmann² made the statement that every albuminous urine contained in addition to serum albumin, serum globulin; in small quantity to be sure, but demonstrable. A little while later Gerhardt,³ in an endeavor to distinguish between renal and febrile albuminuria, discovered in the urine a proteid substance which was not coagulated by boiling. It was present in small quantities in a variety of ailments, especially in those accompanied by high temperatures—diphtheria, typhoid and typhus fevers. Gerhardt designated the condition "latent albuminuria." Subsequent researches confirmed and extended these observations and established the close relation between the "latent albumin" of Gerhardt

and peptone, the product of gastric digestion of albuminous substances. Peptonuria of slight degree was found to be an accompaniment of very many disorders: nephritis, suppurative processes, acute yellow atrophy of the liver, ulcerative diseases of the intestine, including typhoid fever and carcinoma of the bowel; it was described as occurring in scurvy. In short, so manifold were the conditions under which small quantities of peptones were found in the urine that conclusions of much practical value could not be drawn.⁴

With the well-known researches of Kühne and Chittenden⁵ on gastric digestion, the subject of peptonuria entered a new phase. You will recall that they established the existence of a number of products intermediate between albumin properly speaking and peptones, namely, the albumoses. Differing among themselves in some details of solubility, they give certain of the reactions of the albumins and like them are precipitated by ammonium sulphate. Yet they partake of the nature of peptones, for they are not precipitated by boiling and they give the biuret reaction. In the light of Kühne and Chittenden's work, the conclusions concerning peptonuria had to be revised; probably all instances of "peptonuria" in the old sense are, as a matter of fact, examples of albumosuria. Using special methods for their recognition, albumoses have been found in small quantities in the urine of individuals suffering from various acute ailments; most constantly, perhaps, in pneumonia, purulent meningitis and empyema.

Now, this acute, transitory or slight albumosuria cannot be confused with the condition demonstrated to-night. In this second class the presence of a comparatively large amount of an albumose-like substance so alters the behavior of the urine toward the usual reagents that, as you have seen, the condition can be recognized without the employment of a relatively elaborate method. Moreover, in addition to the comparatively excessive degree, the albumosuria is persistent over long periods of time, not transitory.

The first recorded observation in this class was reported by Henry Bence Jones before the Royal Society of London in 1847.⁶ He begins his communication thus: "On the first of November, 1845, I received from Dr. Watson the following note, with a test-tube, containing a thick, yellow semi-solid substance: The tube contains a urine of a very high specific gravity; when boiled it becomes highly opaque, on the addition of nitric acid it effervesces, assumes a reddish hue, becomes quite clear, but, as it cools, assumes a consistence and appearance which you see: heat relieves it. What is it?" Bence Jones then proceeds to tell of his researches. The urine was voided by a grocer 45 years of age who had been "out of health" for thirteen months. The urine showed variations in its coagulability; as a rule it bore brisk and prolonged boiling without coagulating. With

⁴ See Senator, Ueber Peptonurie, *Deut. Med. Wochenschr.*, 1895, Bd. 21, S. 217.

⁵ *Zeitschr. f. Biol.*, 1883, Bd. xix, S. 159, 209; 1884, Bd. xx, S. 11.

⁶ *Phil. Trans. Royal Soc.*, 1848, Pt. 1, p. 55.

² *Virch. Arch.*, 1866, Bd. xxxvi, S. 125.

³ *Deut. Arch. f. Kl. Med.*, 1869, Bd. v. S. 215.

copper sulphate and caustic potash, it gave a claret color. Most characteristic of all, Bence Jones thought, was its behavior toward nitric acid. This reagent gave a precipitate which dissolved on heating and reappeared on cooling. On January 2, 1846, he makes the note that the patient died, adding, "The following day I saw that the bony structure of the ribs was cut with the greatest ease and the bodies of the vertebræ were capable of being sliced off with a knife." . . . "The kidneys were sound both to the eye and microscope."

In 1850 Dr. Macintyre, who had attended the patient, published some details of his illness.⁷ The man dated his ailment from a violent strain he had sustained in September, 1844, in vaulting out of an underground cavern. On coming to the ground he felt as if something "gave away" within his chest, with the further result that he suffered at the time agonizing pain. The pain gradually subsided, but about a month later he was again seized with sharp pain in the chest, this time without an apparent cause. In the following spring he had another severe paroxysm, the pain was referred to the right side between the ribs and the hip and was considered pleuritic in origin. These periods of intense suffering alternated with periods of marked amelioration. In time, however, every movement of the trunk was attended with excessive pain. The poor sufferer became anæmic and lost much weight and strength. Diarrhœa supervened, and finally, after a sixteen months' illness, the patient died exhausted. Physical examination failed to reveal the nature of this painful and fatal illness. The remarkable urinary reactions were noted two days before the specimen was sent to Bence Jones. Post mortem the condition was designated "Osteomalacia fragilis rubra." The substance of the sternum, ribs and vertebræ was rarefied and crumbling; their interior filled with a soft red gelatinous matter which microscopically consisted of "granular matter, oil globules, nucleated cells, constituting the bulk of the mass—a few caudate cells and blood-disks extravasated largely amongst the other cells, and giving the red color to the gelatiniform mass."

Bence Jones' observation was almost forgotten, when in 1883 Kühne⁸ published the result of an examination of urine sent to him in 1869 with a clinical history by Stokvis, a Dutch clinician. In the specimen he rediscovered the reactions of Bence Jones and showed their close relation to those of his own digestive albumoses. The patient died after a nine months' illness which had been diagnosed as osteomalacia, but an autopsy was not held.

Several years elapsed and a third case was described from the clinical standpoint by Kahler and chemically by Huppert.⁹ A physician was the patient, the clinical diagnosis was osteomalacia; the urine afforded Bence Jones' reactions but post mortem instead of osteomalacia, a multiple round-cell sarcoma of the bone-marrow; in other words, a mul-

tiple myeloma was disclosed. Thereupon Kahler suggested that the presence of Bence Jones' reactions might be of service in the diagnosis of multiple myeloma. Might not the other two cases of so-called osteomalacia with albumosuria have been instances of this disease? Bence Jones had recognized that the association of the unusual urinary reactions and the disease of the bone was probably not a fortuitous one, for at the conclusion of his communication he writes: "This substance must again be looked for in acute cases of mollities ossium." But it is Kahler who first identified the pathological condition in these cases of bone disease and albumosuria with the affection previously described by v. Rustizky¹⁰ and called by him "Multiples Myelom." The Italians give Kahler due credit, for Bozzolo's case is presented under the caption "Sulla malattia di Kahler."¹¹ By the accumulation of recorded cases, Kahler's surmise has become a fact.

To be brief, let me say that in the fifty years following Bence Jones' presentation of his case before the Royal Society, there were published and available for criticism only four observations on albumosuria associated with primary bone disease. Within the last three years, however, eight additional cases have been recorded. In eight of the thirteen cases the autopsy has disclosed neoplasms which must be classified as myelomata. In two cases the tumors were visible, in the remainder there was no record of a post-mortem inspection.¹²

In this series are not included two examples of Bence Jones' albumosuria which seem to be exceptions to the general rule, since in one there was no ground (albumosuria excepted) for assuming a disease of the bone, while in the other there were, to be sure, changes in the bone-marrow, but their identity with those found in myeloma could not be satisfactorily established.

The first case is described by Dr. Fitz¹³ as one of myxœdema in which marked and persistent albumosuria was a feature. The patient died while under thyroid therapy. Inasmuch as no autopsy was held, the case is not above criticism. It is in the course of this publication that brief reference is made to the only recorded American observation on multiple myeloma and albumosuria.

Askanazy's case of lymphatic leukæmia¹⁴ constitutes the second apparent exception.

His patient was a man fifty-one years of age, who was ad-

¹⁰ Deut. Zeitschr. f. Chir., 1873, Bd. 3, S. 162.

¹¹ VIII Congresso di medicina interna, 1897, (Transactions).

¹² The cases reported are those of Bence Jones, loc. cit.; Kühne and Stokvis, loc. cit.; Kahler, loc. cit.; Stokvis, quoted by Rosin; Seegelen, Deut. Arch. f. Kl. Med., 1897, Bd. 58, S. 126; Rosin, Berl. Kl. Wochenschr., 1897, Bd. 34, S. 1044; Bozzolo, loc. cit.; Ewald, Wien. Kl. Wochenschr., 1897, S. 169; Bradshaw, Med. Chir. Trans., London, 1899, p. 251; Fitz, Amer. Jour. Med. Sc., 1898, vol. 116, p. 30; Naunyn, Deut. Med. Wochenschr., 1898, Vereins Beilage, S. 217; Ellinger, Deut. Arch. f. Kl. Med., 1899, Bd. 62, S. 255; Sternberg, Nothnagel's Spec. Path. u. Ther., 1899, Bd. vii, Th. ii, Abth. ii, S. 57.

¹³ Loc. cit.

¹⁴ Deut. Arch. f. Kl. Med., 1900, Bd. 68, S. 34.

⁷ Med. Chir. Trans., London, 1850, vol. 33, p. 211.

⁸ Loc. cit.

⁹ Prag. Med. Wochenschr., 1889, Bd. 14, S. 33.

mitted to the hospital in June, 1898. In the summer of 1897 he began to complain of feeling weak; he lost weight and was easily fatigued. Six months later he noted that the cervical glands were enlarging. On admission he was somewhat anæmic; the legs and the abdominal wall were œdematous. There was a moderate enlargement of the lymph glands of the neck and axillæ; several small subcutaneous glands were palpable over the chest wall. A glandular tumor about the size of a man's head occupied the right upper quadrant of the abdomen. Small tumors were felt in Douglas's fossa. The blood showed the changes of lymphatic leukæmia. The urine exhibited Bence Jones' albumosuria. Five weeks later the patient died, and acute pulmonary œdema being the immediate cause of death. At the autopsy the ribs were found very thin; four of them were fractured presumably in transporting the cadaver. A thick, gelatinous marrow, the color of meat, occupied the wide meshes of the bony structure. Microscopically, this marrow was composed of colorless elements, among which the lymphoid cells predominated. There was a hyperplasia of all the lymphatic glands.

Unless the process is to be viewed as a diffuse myeloma, here is an exception. Until the relations of the myelomata to leukæmic and pseudo-leukæmic processes are determined, Askanazy's case must be considered one of lymphatic leukæmia associated with Bence Jones' albumosuria. But this single possible exception need not vitiate the importance of albumosuria as a sign of bone-marrow tumors, seeing that in all other instances where the investigation has been thorough, a multiple myeloma has been the underlying condition.

To demonstrate the converse proposition that all cases of multiple myeloma are accompanied by Bence Jones' albumosuria is not possible, the data being insufficient. Several considerations must be taken into account. The first is the difficulty in deciding just what a myeloma is; a difficulty to which I shall again refer. These urinary reactions seem to be specific for myeloma, not an accompaniment of every bone tumor. At the last German Congress for Internal Medicine Naunyn¹⁵ stated that he had observed a patient whose skeleton was riddled with metastatic carcinomatous growths but the urine failed to give the reactions of Bence Jones.

Furthermore, it must be borne in mind that the time of the appearance of the reactions in the course of the disease has not been definitely determined. In the Stokvis-Kühne case the albumosuria appeared not until the illness was well advanced and disappeared three months before death. But this observation is exceptional; the albumosuria is, as a rule, an early sign and is persistent.

Quantitatively it is subject to great variations. In Ellinger's case the proteid content averaged from $\frac{1}{4}$ to $\frac{1}{2}$ per cent, while in the famous specimen submitted to Bence Jones, it reached the high percentage of six and nine-tenths. Even in the course of any single case there may be marked

remissions in the intensity of the reaction, a fact noted by Matthes¹⁵ and likewise observed in the second case of our series.

It must be shown, then, that the diagnosis of the nature of the bone tumor has been well founded and that repeated urinary examinations have been made before one can accept v. Jakseh's statement that he has observed cases of multiple myeloma in which there was not a trace of albumose in the urine.¹⁶

The exact nature of the substance giving rise to the reactions of Bence Jones has not been determined. All investigators have noted the close relation existing between these reactions and those of the albumoses in Kühne's sense, and yet when isolated it differs in minor features from any of the known digestive proteoses. Recently before the German Congress just referred to, Magnus-Levy¹⁷ denied its albumose character. He stated that he had isolated Bence Jones' proteid in crystalline form; that its property of being dissolved at the boiling-point was not constant; that by the addition of small quantities of salts or extractives such as urea or by slight alterations in the physical conditions its solubility or insolubility at a temperature of 100 degrees could be brought about at will. Moreover, he argued, its structure must be more complex than the albumoses, for as a result of its peptic digestion almost all of the primary split products, namely, the albumoses, were obtained.

The origin of the proteid is as obscure as its character. Ellinger's attempt to extract it from the marrow tumors was not successful. But his demonstration of its presence in the blood is fairly satisfactory. On the other hand, in his case of lymphatic leukæmia Askanazy could not demonstrate the reactions in the blood, yet was successful in finding the proteid in an extract of the bone-marrow. You will see that these are obscure problems requiring further research.

Aside from the reactions to which I have so often referred, there are no constant alterations in the urine. Kahler's patient voided 2,230 cc. in 24 hours, but he was accustomed to drink large quantities of alkaline water. Otherwise there is no reference to a polyuria comparable to that exhibited by Dr. Iglehart's patient.

Bradshaw's patient voided a milky urine from time to time for a year previous to the onset of any localizing symptoms.

Besides the peculiar albuminose proteid the urine usually contains albumin in traces. In Senator's case¹⁸ there was a coexisting nephritis manifesting itself by the presence in the urine of numerous casts and albumin. At the autopsy the kidneys were large and had suffered fatty and amyloid degenerations. Needless to add that a myeloma was also disclosed.

I pass now to a more accurate description of the nature of myelomata. Multiple new growths of the bone-marrow, they do not correspond to the usual conception of malignant

¹⁵ Verhand. d. Cong. f. inn. Med., 1900, S. 496, et. seq.

¹⁵ Loc. cit.

¹⁶ Loc. cit.

¹⁷ Loc. cit.

¹⁸ See Rosin, loc. cit.

neoplasms in the Cohnheim sense, inasmuch as they probably never metastasize.

The name "multiple myeloma" originated with v. Rustizky,¹⁹ who viewed the process as a simple hypertrophy of the bone-marrow, and for these reasons: the tumors were present only in the bones and, indeed, originated only in the bone-marrow, that although multiple, they did not metastasize; therefore, did not belong to the class of malignant neoplasms. Since v. Rustizky's publication there have been several attempts to gather together the scattered records of apparently similar growths.²⁰ Thus there have been collected examples of diseases of the bone with most diverse titles—osteomalacia, medullary pseudo-leukæmia, sarcomatous osteitis, malignant osteomyelitis, lymphosarcoma. Histologically in the majority of instances the structure has been that of a round-cell sarcoma. Recently, Wright²¹ has described a myeloma in detail in connection with Fitz's case. The tumor elements, according to his research, really form a variety of plasma cells. A myeloma does not originate in the marrow cells as a whole, but in only one of its elements, the plasma cell. Following the results of this important contribution, the tumor may be classed as a plasmoma.

In gross, these tumors form masses of soft reddish tissue of various sizes, often ill-defined, replacing the normal marrow and osseous substance. The sternum, ribs, vertebrae and skull are prone to the affection though all the bone may be involved. The tumors may or may not appear on the exterior. The bones are softened and apt to suffer pathological fractures with resulting deformities. These facts of pathological anatomy explain in part the varying clinical pictures of multiple myeloma.

A disease of later life, it affects males more frequently and runs its course as a rule within two years. Bozzolo's patient lived four years after the onset of the first symptoms, while the physician under Kahler's care suffered eight years before death relieved him. The recital of this history makes a harrowing tale, but as it serves to illustrate one type of the disease I shall present it in some detail:

Dr. Loos was in 1879 a well-developed man, 46 years of age, of healthy appearance. In July of that year he was suddenly seized with severe pain in the upper half of the chest on the right side. A brother physician examined him but could not detect any abnormality. In the course of a week he felt entirely well. The following December, suddenly and without apparent cause, he had another similar attack of intense pain. This time, however, it was distinctly localized in an exquisitely tender area over the third right rib in front. But just as before, the pain soon disappeared. The urine at this period presented no abnormal change.

During the year 1880 paroxysms of intense pain, referred

to numerous ribs and other parts of the trunk as well as to the right patella, alternated with periods of comfort, during which he could attend to his busy practice. Any unusual muscular exertion, however, would call forth violent pain.

In March, 1881, following a slight contusion, an exceedingly painful and tender area appeared over the fifth left rib. A flat elevation could be outlined over the costal surface, but in the course of a few weeks both pain and elevation had disappeared only to recur later in other ribs and bones. During the latter part of this year and for the first time, the urine gave a heavy precipitate with nitric acid. The patient had lost considerable weight and looked ill.

The early months of 1882 were passed in much the usual way. When confined to bed by the unbearable bone pain and neuralgias his condition was truly pitiful. Every movement aggravated and intensified his great suffering. Besides, his nights were sleepless and paroxysms of tachycardia and cardiac oppression added to his discomfort. The summer of this year saw an improvement so that he was able to resume to some extent his favorite pastime, hunting. But the improvement was temporary, for before the year closed the painful attacks returned, the anginal paroxysms were renewed and in addition he was troubled with nausea.

The poor doctor's suffering continued during the following two years, 1883 and 1884. What with the pain in the ribs and sternum, the anginal attacks and nausea, paresthesias in the lower limbs, visceral pains and obstinate insomnia, his state had become deplorable.

In 1885 a kyphotic bowing of the upper thoracic vertebral column was noted. In December of this year Kahler saw him for the first time. He was then cachectic; his spinal column presented a dorsal kyphosis. Standing, his face pointed down; the trunk appeared markedly shortened compared with the length of the extremities. There was marked tenderness on palpating certain circumscribed areas over the body of the sternum and the ribs. Careful and repeated examinations of these regions disclosed very slight elevations of the bony surfaces. The urine exhibited the reactions of albumosuria.

The doctor's condition grew progressively worse in 1886. Pain recurred in various bones of the trunk and neuralgias in the nerves of the extremities. The kyphosis increased, the thorax became deformed, the sternum projecting forward and the ribs appearing correspondingly bent. In 1887 the inguinal glands were found enlarged. The sense of hearing had been diminishing for several years, but now its impairment was very marked. A double labyrinthine affection was diagnosed. In April of this year a well-marked crepitus could be elicited over the third right rib by pressure and by the respiratory movements. A tumor appeared in the right supraspinous region.

Finally, deformed, deaf and suffering, the patient was released by death in August, 1887.

I have spoken of the clinical diagnosis in the case as well as the anatomical examination. The essential features of this type of the disease are the paroxysms of pain referred

¹⁹ Loc. cit.

²⁰ See Hammer, Virch. Arch., 137, S. 200.

²¹ Contributions to the Science of Med. dedicated to Dr. W. H. Welch. The Johns Hopkins Press, Baltimore, 1900.

to the bones, the great deformity of the skeleton of the trunk, the cachexia and the presence of Bence Jones' albumosuria. These are the cases that have been mistaken for osteomalacia, but in no example of true osteomalacia have these urinary reactions been discovered, so that the albumosuria suffices for differentiation.²²

The patient shown you to-night illustrates a second class. Here the tumors are visible and there are pathological fractures. In Bozzolo's patient the tumors appeared on the arms, shoulders and ribs. A diagnostic difficulty arises in deciding whether these tumors are metastases of a primary growth latent in some distant organ or multiple primary tumors of the bone. The albumosuria not only answers this question but at the same time determines the nature of the new growth. In no instance of multiple metastatic osseous tumors have Bence Jones' reactions been present and the new growth has invariably been a myelogenous sarcoma, a myeloma.

In a third division must be placed the cases of multiple myeloma in which the bone symptoms and signs are vague or even absent. To this class belongs the case of Ellinger:

His patient was a man 45 years of age who was admitted to Lichtheim's clinic in October, 1897. For about six weeks he had had, almost daily, chilly sensations, fever and sweats. His appetite failed and he felt ill. He did not complain of pain in any part of the body.

The man was fairly well nourished and presented slight jaundice and fever. The urine contained some albumin and biliary pigments. The jaundice diminished but the fever persisted; the patient grew weaker and paler. Four weeks after admission Bence Jones' reactions were discovered in the urine. Two weeks later the clinical picture was clearly one of progressive anæmia with hemorrhagic sputum and effusions into the subcutaneous tissue, the joints and serous cavities. In a few days this condition led to the exitus lethalis. Just before death it was noted that percussion over the sternum was painful. No diagnosis was made. Post mortem, a multiple myeloma was discovered.

In cases such as Ellinger's the progressive anæmia and its concomitants occupy the attention of the observer, and, unless the significance of the albumosuria is recognized, a diagnosis is impossible.

A transition from this class of multiple myeloma to those in which the bone lesions are evident is illustrated by Dr. Iglehart's patient. Macintyre's case, which formed the basis of Bence Jones' observations, belongs to this variety of myeloma. Macintyre wrote that "the affection to which it bore the nearest resemblance was a severe attack of lumbago or sciatica." But he adds it was evident "that suffering so intense must have a deeper seat and more formidable cause than mere muscular or neuralgic rheumatism." In discussing the diagnosis of maladies of the bone, he remarks that their nature is usually not suspected until they are fully developed and until deformities or fractures are present. He adds very wisely: "It is this considera-

tion that, in my mind, invests the properties of the urine, voided by this patient, with their chiefest interest."

In relating the clinical histories of multiple myelomata, I have mentioned several of the anomalous symptoms—fever, nausea, attacks of visceral pain, neuralgias and paresthesias.

The remarkable nervous symptoms have been considered in detail by Senator.²³ His patient presented a double hypoglossal paralysis, anæsthesia in the region supplied by the third division of the trigeminal nerve and a paresis of the arytenoideus. These curious phenomena so dominated the clinical aspect of the case that in spite of the presence of albumosuria a diagnosis was not reached. The autopsy disclosed myelomata, but no appreciable change in the nervous system was found. Senator regards the anæmia in such cases as the etiological factor, basing his opinion on the researches which have demonstrated that not only slight functional disturbances in the nervous system but even gross alterations in its structure may occur in the course of a profound anæmia.

I have attempted to show you how manifold is the symptomatology of multiple myeloma. You may readily imagine the obscurity of the cases in which the osseous system presents no localizing symptoms.

It is as a contribution to the diagnosis of these obscure cases of a pernicious bone disease that I have presented this preliminary report and emphasized the importance of Bence Jones' albumosuria.

DISCUSSION.

DR. WELCH.—The most interesting recent contribution to the pathological anatomy of so-called multiple myelomata is the paper of Dr. James H. Wright, to which Dr. Hamburger has referred. It seems clear that the lesions of the bones in this disease are not genuine tumors in the Cohnheim sense, and that the multiple nodules are not to be regarded as metastatic tumors secondary to a primary one. The growths in the bones have much in common with the infectious tumors. In the case reported clinically by Dr. Fitz and anatomically by Dr. Wright, the tumor-cells were predominantly plasma cells. It remains for future investigations to determine whether in all cases these multiple myelomata, which, as well known, have been described under a great variety of names, present the special histological characters so well described by Dr. Wright. If so, they would belong to the class of new growths, first designated by Unna as plasmomata. To this class belong many of the so-called infectious granulomata.

I have recently examined a small tumor of the palpebral conjunctiva sent to me for diagnosis and have found that the tumor is composed almost wholly of plasma cells, mixed with so few ordinary lymphoid cells that transitions between the latter and plasma cells are not easy to find. Probably some of the tumors which we formerly were accustomed to

²² See Kahler, loc. cit.

²³ Berl. Kl. Wochenschr., 1899, Bd. 36, S. 161.

diagnose as lympho-sarcoma, round-celled sarcoma, etc., will be found to be plasmomata.

DR. ATKINSON.—Have these cases of albumosuria with bone lesions any connection with the cases of osteitis deformans reported some years ago by Paget and recently by Smith (*Ergebnisse der Allgemeinen Pathologie und Pathologischen Anatomie des Menschen und der Thiere*); the disease coming on insidiously with enlargement of the bones, gradual increase in the size of the head and shortening of the body through degeneration of the bones and bowing of the legs? In a certain number of those cases of osteoporosis

and osteosclerosis the end has been cancer of the bones, and I suspect albumosuria might have been found if looked for. I saw last spring an individual with typical osteitis deformans but he showed no lumps on the bones and no such reaction in the urine.

DR. HAMBURGER.—I know of no relation between the two conditions and of no literature on the subject.

NOTE.—The colored woman died February 1, 1901. Post mortem, myelomata were found in the skull, left scapula, both clavicles, the sternum, the right ilium and neck of the right femur.

Examination of Dr. Iglehart's patient now shows a slight but definite elevation over the ninth left rib in front.

REPORT OF A CASE OF FULMINATING HEMORRHAGIC INFECTION DUE TO AN ORGANISM OF THE BACILLUS MUCOSUS CAPSULATUS GROUP.

BY GEORGE BLUMER, M. D., AND ARTHUR T. LAIRD, M. D.

(From the Bender Hygienic Laboratory, Albany, N. Y.)

The subject of hemorrhagic infection in man, due to organisms of the *Bacillus mucosus capsulatus* group, has been so recently discussed in this country by Howard¹ that it seems hardly necessary to more than briefly review the subject in reporting a new case. The cases hitherto reported have varied from one another to a considerable degree in their intensity, and to a certain extent in the character of their lesions. Whilst in some cases the lesions were purely septicæmic and the infection of the cryptogenic type, in other instances the process seems to have started as a local infection, though quickly becoming generalized. Thus the cases of Bordoni-Uffreduzzi,² Von Dungern³ and Kolb⁴ were of the character of general infections without special points of origin, the cases of Tizzoni and Giovanni⁵ seemingly originated from the skin, those of Babes⁶ from the bronchi, and in our own case the intestinal tract was in all probability the primary seat of infection. In all instances the essential feature of the process was its hemorrhagic character.

The following case occurred in the practice of Dr. D. L. Kathan of Schenectady, to whom we are indebted for the history, and who kindly obtained permission for the autopsy. The case seems worthy of record on account of the relative rarity of this form of disease.

A. F., aged 20, a machinist.

Family History.—His father died of cancer of the kidney at 55. His mother died of pulmonary tuberculosis at 30. Two sisters are alive and well. There are none dead in the family.

Past History.—The patient has always been unusually strong and athletic. His habits are excellent.

Present History.—The patient had been in perfect health and working every day until October 19, 1900. On the morning of that day he went to work as usual after a hearty breakfast. He returned just after noon, not having eaten his dinner. He complained of feeling ill, and went directly to bed. He began to vomit and purge, the bowels moving every few minutes. He complained of pain in the abdomen. Examination showed that there was no local abdominal tenderness, no tympanites. The temperature was 103° F. The pulse was 120.

At the end of twelve hours he was seen again. At that time the bowels were only moving about once in four hours, and the vomiting had practically ceased. The temperature was subnormal. The hands and feet were cold and cyanosed. The face had a pinched appearance.

At the end of 24 hours there was confusion of mind, and the patient was in a state of complete collapse. Death occurred at the end of 36 hours, there having been at no time the slightest tendency towards recovery.

The autopsy was made six and a half hours after death in cool weather.

The following notes are abstracted from the protocol:

The body is 171 cm. long, powerfully built, and well nourished. Rigor mortis is well marked. There is extensive post-mortem lividity of the legs, arms and trunk. The surface is pale; there is no œdema. The lips and finger-tips are cyanotic. The mucous membranes are pale. The muscles are exceptionally well developed and normal looking. The peritoneal cavity is dry, both layers of the peritoneum being smooth. The omentum and appendix are normal.

The heart is in every way normal except for the presence of numerous subepicardial hemorrhages of small size, and slight cloudy swelling of the musculature.

¹ Howard: *Journal of Experimental Medicine*, vol. iv, No. 2, 1899.

² Bordoni-Uffreduzzi: *Zeitschrift für Hygiene*, 1888, Hft. iii.

³ Von Dungern: *Centralblatt für Bakteriologie*, Bd. xiv, No. 17, 1893.

⁴ Kolb: *Arbeiten aus den Kaiserliche Gesundheitsamte*, Bd. vii, 1891.

⁵ Tizzoni and Giovanni: *Ziegler's Beiträge*, vi, p. 201, 1889.

⁶ Babes: *Archives de Médecine Expérimentale*, tome v, 1890.

The lungs show numerous subpleural hemorrhages with congestion, and a few elevated, finely granular, deep-red areas, suggesting fresh broncho-pneumonia.

The spleen is much enlarged, measuring $16 \times 10.5 \times 5$ cm. On section it shows numerous hemorrhages into the pulp, and marked swelling of the Malpighian bodies.

The liver is enlarged, soft, and markedly cloudy.

The kidneys both present the same appearances, being much softer than normal, with their cortices pale and swollen. There are a few submucous hemorrhages beneath the mucous membrane of the pelvis.

The adrenals, bladder, prostate and pancreas are normal.

The stomach shows a few submucous hemorrhages, but is otherwise normal.

The solitary follicles throughout the small intestine are markedly swollen, and in the ileum Peyer's patches are also affected. The mucosa of the intestine between the swollen lymphatic apparatus is congested and in places markedly hemorrhagic; in places the Peyer's patches contain discrete hemorrhages.

The large intestine is normal.

The mesenteric glands are swollen, some of them being pale, others hemorrhagic.

The brain and cord could not be examined.

MICROSCOPIC EXAMINATION.

The heart-muscle shows nothing beyond an excessive number of polymorphonuclear leucocytes in the vessels.

The lung shows in places groups of alveoli containing red blood-corpuscles, with a few desquamated epithelial cells and an occasional dust cell. The blood-vessels in this organ also contain an excessive number of polymorphonuclear leucocytes.

The liver shows marked cloudy swelling of its cells, with occasional single-cell necroses. The portal vessels contain a great excess of leucocytes, which have wandered out in quite large numbers into the periportal connective tissue.

The spleen shows great dilatation of all its blood-spaces with blood. In the pulp spaces many large phagocytic cells containing red corpuscles are made out. There is no distinct evidence of proliferation of the endothelial cells lining the splenic vessels.

The kidneys show marked cloudy swelling of the parenchymatous cells. The capillaries, especially those of the glomeruli, are crowded with polymorphonuclear leucocytes. Two distinct types of localized lesions are to be made out in these organs. In places in the cortex are localized collections of polymorphonuclear leucocytes invading the tubules and the intertubular connective tissue. In the medulla near its junction with the cortex are areas in which the intertubular connective tissue is quite oedematous-looking, and is infiltrated with a few polymorphonuclear leucocytes, and a moderate number of cells with round extracentral nuclei which have the staining reactions of plasma cells. These cells evidently come from the neighboring blood-vessels

which contain many of them. No casts are seen in the tubules.

The changes in the intestines are partly inflammatory and partly proliferative in character. The inflammatory changes are most marked in the interglandular tissue and consist in an infiltration with polymorphonuclear leucocytes accompanied by hemorrhage. The proliferative changes are most marked in the lymphatic apparatus. They consist in the appearance of large cells of an endothelial type amongst the lymphoid cells which are greatly decreased in number. These large cells have distinct phagocytic properties and contain in places deeply stained particles of nuclear substance, presumably portions of lymphoid-cell nuclei. The blood-vessels in and near the lymphatic apparatus show proliferative changes in their endothelium. The proliferated cells almost block the capillaries in places, whilst in other places fibrin-formation with complete thrombosis has occurred. The changes resemble in every way those described by Mallory in typhoid fever, though less in degree.

The changes in the mesenteric lymph glands are essentially the same as those in the lymphatic apparatus of the intestine.

Sections of the various organs examined for microorganisms show short thick bacilli in the blood-vessels of the lung and in the areas containing exudate. They are also found in the sections of intestine and in the mesenteric glands. The organisms are, as a rule, free between the cells, but occasionally are found in large numbers in polymorphonuclear leucocytes. These organisms resemble those subsequently isolated from the mesenteric glands and the lung.

Cultures were made at the time of the autopsy from the heart's blood, lung, liver, spleen, bile and a mesenteric lymph gland.

All of these remained sterile after several days in the thermostat at C. 37° ; except the culture from the lung, and that from the mesenteric gland. The tubes from each of these organs showed numerous colonies of a single organism which presented the following morphological and cultural characteristics. Unless otherwise stated, cultures were made on standardized media with an acidity of 1.5 according to Whipple's scale:

Morphology.—In young cultures grown at the temperature of the thermostat the organism appears as a bacillus, varying from 1 to 4 microns in length and averaging 0.5 micron in width. The organisms occur singly or in pairs or chains of 2 or 3 elements. The ends are rounded, many of the short forms appearing almost oval. Occasional thread-like forms are observed. Irregularly shaped forms, which stain unevenly, are seen in old potato cultures (6 days at C. $36-38^{\circ}$). The organism stains well with aqueous methylene blue (1:9), better with Löffler's methylene blue. Bipolar staining is sometimes noticed in the short forms. The organism is decolorized by Gram's method.

A capsule is to be made out by Wele's method in smears from animal tissues, and is occasionally seen in blood-serum cultures; it is not uniformly present.

No spore-formation is observed.

Flagella are not present, and the organism seems to be non-motile.

The organism grows best aërobically, but is also capable of growth under anaërobic conditions. It grows on media as follows:

Agar Slant.—After 24 hours there is a luxuriant, elevated, porcelain-white growth along the line of inoculation; the edge is finely serrated. There is abundant growth in the water of condensation. The growth is not markedly viscid. It has no odor.

Agar Plates.—The superficial colonies are circular, elevated, about 2 mm. in diameter with a sharply defined margin and a snow-white color. Under the low power they are made up of a coarsely granular periphery surrounding an opaque center. The deep colonies are spherical or lens-shaped, white, about 0.5 mm. in diameter, and microscopically finely granular in structure.

Gelatin Plates.—The surface colonies are small, not more than 1 mm. in diameter; they show little tendency to spread and are circular, elevated, white, and denser at the center than at the periphery. Under the low power they are yellowish, coarsely granular, and show a concentric arrangement and finely serrated edges. The deep colonies are spherical, opaque and finely granular.

Gelatin Stab.—There is a delicate growth along the line of the stab, and a slight circular non-elevated growth on the surface. No liquefaction is produced.

Potato.—After 24 hours there is a luxuriant, spreading, moist, elevated, brownish-yellow growth. The potato is discolored a brownish yellow. There is no gas production.

Dunham.—Is uniformly cloudy after 24 hours. No pellicle is formed. Later there is an abundant grayish-white sediment, which on agitation diffuses evenly through the liquid, and is not stringy.

Blood-serum.—The growth is similar to that on agar. There is no liquefaction of the medium.

Indol-Formation.—The organism produces indol in dextrose free bouillon after 4 days at C. 37°.

Gas-Formation.—Several different tests were made with each medium. Gas noted after 72 hours at C. 37°.

In 1 per cent glucose bouillon, 45-60 per cent of gas.

$\text{CO}_2^{\frac{1}{3}}$

$\text{H}_2^{\frac{2}{3}}$

In 1 per cent lactose bouillon, 45-55 per cent of gas.

$\text{CO}_2^{\frac{1}{4}}$

$\text{H}_2^{\frac{3}{4}}$

In 1 per cent saccharose bouillon, no gas is found as a rule. On one occasion a trace was noticed.

Pathogenesis.—25 minims of a 72-hour bouillon culture were injected subcutaneously into the abdominal wall of a full-grown guinea-pig. The animal died within 24 hours. The autopsy showed slight swelling at the point of inoculation, swelling of the nearest lymph glands with hemorrhages, an early serofibrinous peritonitis, and hemorrhages into the kidneys and beneath the pleura. The intestinal lymphatic

apparatus was swollen and surrounded by congested mucous membrane. The organism was found in coverslips from the point of inoculation and the blood, at times encapsulated. It was recovered in pure culture from the seat of inoculation, blood and spleen.

25 minims of a 72-hour bouillon culture were inoculated into the peritoneal cavity of a full-grown guinea-pig. The animal died within 24 hours. The autopsy showed that there was no local or glandular reaction. There was a distinctly viscid seropurulent peritoneal exudate. The spleen was enlarged. There were hemorrhages into the adrenals and beneath the pleura. There was a fresh right-sided pleurisy. The organism was seen in the smears from the blood and peritoneal cavity, many of the organisms from the latter place having a distinct capsule. It was recovered in pure culture from the heart's blood, spleen and peritoneal exudate.

A full-grown rabbit was inoculated into the ear-vein with 25 minims of a 72-hour bouillon culture. It died within 20 hours. The autopsy showed no reaction at the point of inoculation. There was a fresh fibrinous peritonitis. The spleen was enlarged, soft and congested. The liver and kidneys were also congested, as was the mucous membrane of the uterus. The organism was recovered from the heart's blood, spleen and peritoneum in pure culture.

Anatomical Diagnosis.—Hemorrhagic infection due to an organism of the *Bacillus mucosus capsulatus* growth; acute hemorrhagic follicular enteritis; acute spleen tumor with swelling of the Malpighian bodies; cloudy swelling of the liver and heart muscle; acute infectious and interstitial nephritis; hypostatic congestion of the lungs.

We have placed the organism isolated in this case in the group of *Bacillus mucosus capsulatus*, since whilst it differs in minor points from similar organisms already described, it corresponds in the following features laid down by Fricke¹ for the identification of members of this group. Howard, quoting from Fricke, states as follows:

"The more important common characteristics of this group are the morphology, plump, medium-sized, pleomorphic rods; the presence of capsules, readily demonstrable in the animal body and sometimes in cultures; lack of motility and of spores; failure as a rule to stain by Gram; the rapid, luxuriant, elevated, viscid white growth upon the surface of solid media; absence of liquefaction of gelatin; and pathogenicity, usually in the form of septicæmia, but with striking variations for different animals, and for different members of the group."

In comparing this organism with a culture of Howard's bacillus of hemorrhagic septicæmia which he kindly sent us, and with a culture of Pfeiffer's capsulated bacillus, which we obtained from the Laboratory of Hygiene of the University of Pennsylvania, the growth of the three organisms on ordinary media was almost identical. Our organism, however, failed to produce gas in saccharose bouillon, and

¹ Fricke: Zeitschrift für Hygiene, Bd. xxiii, 1896.

produced indol constantly. Both Pfeiffer's and Howard's organisms produced abundant gas in saeccharose bouillon. We were never able to detect indol in cultures of Pfeiffer's organism, though in one out of several cultures of Howard's bacillus we obtained a faint indol reaction. Pfeiffer's organism was furthermore distinguished by the fact that on solid culture media the growth constantly exhibited a mucilaginous consistency so that it adhered to the needle and pulled out into threads. In its failure to produce gas in saeccharose bouillon our organism seems to differ from all of the so far

recorded ones. The various organisms of this group studied by Strong⁸ all produced gas in saeccharose, as did the organisms recently studied by Howard.⁹

The case is of interest pathologically on account of the proliferative changes in the lymphatic apparatus of the intestine, and clinically on account of its exceedingly rapid course.

⁸ Strong: *Journal of the Boston Society of the Medical Sciences*, vol. iii, 1899.

⁹ Howard: *Journal of Experimental Medicine*, vol. v, no. 2, 1900.

INTRODUCTORY NOTE TO DRS. DURHAM AND MYERS'S REPORT.

The following short summary was sent to me by Dr. Durham with the suggestion that it appear in a medical journal in this country. In justice both to the English Commission and to the American Commission, it should be stated that the comment in paragraph 11 is made without knowledge of the later fuller experiments and important results recently published by the latter commission.

Dr. Durham and Dr. Myers spent several days in Baltimore last July on their way to Pará, Brazil. All of us who met these gifted young investigators retain the pleasantest remembrance of them personally and were impressed with their fitness in scientific training and ability for the work which they were about to undertake. A little over a month ago came the sad news that Dr. Myers had succumbed to an attack of yellow fever. Dr. Durham, who contracted the disease at the same time, has fortunately recovered, and at the date of his writing (January 29) was about to resume the study of yellow fever.

The death of Dr. Myers at the outset of his career is a severe loss to medical science. His published contributions show thorough scientific training and marked originality, and, although extending over a period of only about three years, are valuable additions to knowledge, giving promise of much fruitful activity as an investigator. They relate mainly to problems of immunity, especially to immunity from snake-venom and from proteids.

Both Lazear of the American and Myers of the English Yellow Fever Commission have laid down their lives in the search for means of prevention, based upon better knowledge of the causation, of one of the most baffling and terrible scourges of mankind. How much more glorious is the cause to which these bright young lives were sacrificed than any for which nations are in arms to-day!

WILLIAM H. WELCH.

ABSTRACT OF INTERIM REPORT ON YELLOW FEVER BY THE YELLOW FEVER COMMISSION OF THE LIVERPOOL SCHOOL OF TROPICAL MEDICINE.

BY HERBERT E. DURHAM AND THE LATE WALTER MYERS.

NOTE.—The completion of the interim report of which this is an abstract was interrupted by the onset of attacks of yellow fever in both of us. The loss of my much lamented colleague renders it advisable to submit this shortened report only for the time being.—H. E. D.

1. Sufficient search reveals the presence of a fine, small bacillus in the organs of all fatal cases of yellow fever. We have found it in each of the 14 cadavers examined for the purpose. In diameter the bacillus somewhat recalls that of the influenza bacillus; as seen in the tissues, it is about 4μ in length.

2. This bacillus has been found in kidney, in spleen, in mesenteric, portal and axillary¹ lymphatic glands taken from yellow-fever cadavers directly after death. In the contents of the lower intestine apparently the same bacillus is found often in extraordinary preponderance over other micro-

¹ We find these constantly enlarged and much injected, though whether this is specific we are not able to say.

organisms. Preparations of the pieces of "mucus," which are usually if not always present in yellow-fever stools, at times may present almost the appearance of "pure culture."

3. Preparations of the organs usually fail to show the presence of any other bacteria, whose absence is confirmed by the usual sterility of cultivation experiments.

4. It is probable that this same bacillus has been met with, but not recognized, by three other observers. Dr. Sternberg (*Report on Etiology and Prevention of Yellow Fever*, 1890) has mentioned it, and he has also recorded the finding of similar organisms in material derived from Drs. Domingos Freire and Carmona y Valle, but he did not recognize its presence frequently, probably on account of the employment of insufficiently stringent staining technique.

5. It is probable that recognition has not been previously accorded to this bacillus by reason of the difficulty with which it takes up stains (especially methylene blue), and by

reason of the difficulty of establishing growths on artificial media.

6. The most successful staining reagent is carbolic fuchsin solution (Ziehl), diluted with 5 per cent phenol solution (to prevent accidental contamination during the long staining period); immersion for several hours, followed by differentiation in weak acetic acid. Two-hours staining period may fail to reveal bacilli, which appear after 12 to 18 hours. The bacilli in the stools are often of greater length than those in the tissues, and they may stain rather more easily; naturally the same is true of cultures. Some of our specimens have already faded.

7. Since the bacilli are small and comparatively few in numbers, they are difficult to find. To facilitate matters at our last two autopsies (14th and 15th), a method of sedimentation has been adopted. A considerable quantity of organ juice is emulsified with antiseptic solutions, minute precautions against contamination and for control being taken; the emulsion is shaken from time to time and allowed to settle. The method is successful and may form a ready means of preserving bacteria-containing material for future study. The best fluid for the purpose has yet to be worked out; hitherto normal saline with about $\frac{1}{5}$ per cent sublimate has been employed.

8. Pure growths of these bacilli are not obtained in ordinary aerobic and anaërobic culture tubes.

9. Some pure cultures have been obtained by placing whole mesenteric glands (cut out by means of the thermocautery) into broth under strict hydrogen atmosphere. In-

vestigation into the necessary constitution of culture media for successful cultivation is in progress.

10. Much search was made for parasites of the nature of *protozoa*. We conclude that yellow fever is not due to this class of parasite. Our examinations were made on very fresh organ juices, blood, etc., taken at various stages of the disease, with and without centrifugalization,² and on specimens fixed and stained in appropriate ways. We may add that we have sometimes examined the organs in the fresh state under the microscope within half an hour after death.

11. The endeavor to prove a man-to-man transference of yellow fever by means of a particular kind of gnat by the recent American Commission is hardly intelligible for a bacillary disease. Moreover, it does not seem to be borne out by their experiments nor does it appear to satisfy certain epidemiological conditions. It is proposed to deal more fully with the endemology and epidemiology of the disease on a later occasion.

12. We think that the evidence in favor of the etiological importance of the fine small bacillus is stronger than any that has yet been adduced for any other pretended "yellow-fever germ." At the same time there is much further work to be done ere its final establishment can be claimed. The acquisition of a new bacterial intestinal inhabitant would explain the immunity of the "acclimatised."

Pará, Brazil, January 28, 1901.

² We have found this sometimes useful in examining the blood of ague patients.

SUMMARIES OR TITLES OF PAPERS BY MEMBERS OF THE HOSPITAL AND MEDICAL SCHOOL STAFF APPEARING ELSEWHERE THAN IN THE BULLETIN.

IRVING P. LYON, M. D. Types of Normal and Morbid Blood.—*Park's Surgery by American Authors*, Second Edition, 1899.

Colored blood-plate showing types of normal and pathological blood, with description.

GUY L. HUNNER, M. D., and IRVING P. LYON, M. D. Mensuration and Capacity of the Female Bladder. Observations on the female bladder dilated by atmospheric pressure in the knee-breast posture.—*The Journal of the American Medical Association*, December 16, 1899.

(This article is not identical with the article of the same title which appeared in the BULLETIN in December, 1899. It is a longer and fuller article, from which the other was abridged.)

IRVING P. LYON, M. D. On Peculiar Condition of the Hair.—*The Journal of Tropical Medicine*, August, 1900.
[On Plica Polonica.]

CHARLES CARY, M. D., and IRVING P. LYON, M. D. Primary Echinococcus Cysts of the Pleura. Report of a case of primary exogenous echinococcus cysts of the pleura, showing hyaline degeneration of the cuticle without lamellation, with notes from the literature.—*Transactions of the Association of American Physicians*, Washington, Vol. XV, 1900, and *American Journal of the Medical Sciences*, October, 1900.

IRVING P. LYON, M. D., and ALFRED B. WRIGHT, Stud. Med. An Inquiry into the Existence of Autochthonous Malaria in Buffalo and its Environs. Preliminary report on species of mosquitoes and blood-examinations.—*Buffalo Medical Journal*, November, 1900.

THE JOHNS HOPKINS HOSPITAL BULLETIN.

The Hospital Bulletin contains details of hospital and dispensary practice, abstracts of papers read, and other proceedings of the Medical Society of the Hospital, reports of lectures, and other matters of general interest in connection with the work of the Hospital. It is issued monthly.

Volume XI is complete with the present number. The subscription price is \$1.00 per year. The set of eleven volumes will be sold for \$22.00.

NOTES ON NEW BOOKS.

Disinfection and Disinfectants. A treatise upon the best known disinfectants, their use in the destruction of disease germs, with special instruction for their application in the commonly recognized infectious and contagious diseases. By H. M. BRACKEN, M. D., Minnesota State Board of Health. (Chicago, Illinois: The Trade Periodical Company, 1900.)

This little volume is most valuable. It is a manual containing careful and specific directions for the disinfection of clothing, rooms, patients, dead bodies and discharges from the bodies of the sick. It has a chapter with complete and varied information concerning the more common infectious diseases. Specific directions are also given for the proper isolation and care of smallpox, yellow-fever, tuberculous and other patients suffering from infectious diseases. There is no manual in English which contains similar practical information.

Fractures. By CARL BECK, M. D., Visiting Surgeon to St. Mark's Hospital and to the German Poliklinik—with 178 illustrations. (Philadelphia: W. B. Saunders & Co., 1900.)

In this volume of 335 pages the writer has attempted to deal with the general subject of fractures considered mainly from the standpoint of the Röntgen ray. In fact the volume is dedicated to Professor Röntgen. The introductory chapter deals with the general properties of the X-rays and their adaptability to certain varieties of fractures.

Part I deals with the classification, signs, diagnosis and treatment of fractures in general, with some special reference to the process of repair of fractures and disturbances in these processes. In connection with the subject of compound fractures the author discusses in some detail the general principles of aseptic surgical technique; a few pages are also devoted to the peculiarities of fractures in children.

Part II deals with fractures of special regions. Fractures of the shoulder and upper extremity are discussed in considerable detail, especial attention being devoted to fractures of the elbow joint and Colle's fracture. Fracture of the pelvis and lower extremity are also treated of in some detail. The writer especially advises the ambulatory treatment of fractures of the neck of the femur, the leg being immobilized by a plaster of Paris dressing extending from the foot to the pelvis.

A chapter is devoted to fractures of the bones of the trunk and another to fractures of the skull. In the latter the differential diagnosis of injuries to the head is considered and the technique of operation for fracture of the skull discussed.

The volume contains an appendix on the practical use of the Röntgen rays, in which the general principles of X-ray photography as well as the more desirable varieties of apparatus are considered. Considerable attention is devoted to the technique of X-ray photography.

The value of skiagraphy in the diagnosis of obscure lesions of certain organs and viscera is considered, especial attention being devoted to the diagnosis of biliary calculi. The appendix closes with a brief chapter on the errors of skiagraphy.

The volume is by no means an exhaustive discussion of the subject of fractures, and in matters of treatment leaves much to be desired.

The illustrations are numerous and are for the most part taken from skiagraphs, some of which are very good while others are decidedly unsatisfactory. There is in places a decided ambiguity as to the author's meaning, as for instance in discussing fractures of the diaphysis of the femur the following sentence occurs:

"Generally the lower fragment is rotated outward and pulled upward and to the inner and outer side of the upper one."

There is also an evident attempt throughout the volume to

dispense with the time honored terminology of "ical" and to replace it with "ic." In this attempt there is, however, a most decided inconsistency, for in the same sentence the author uses in connection with the same noun the adjectives "chemic" and "mechanical," and in another place the adjectives anatomic and surgical are used in the same sentence.

The Treatment of Fractures. By CHARLES LOCKE SCUDDER, M. D., Surgeon to the Massachusetts General Hospital, Out-Patient Department, etc., assisted by FREDERIC J. COTTON, M. D. With 585 illustrations. (Philadelphia: W. B. Saunders, 925 Walnut St., 1900.)

A carefully prepared work upon a subject of such general interest and importance should be most cordially welcomed by the profession.

In this volume of 433 pages with 585 illustrations the author has treated the subject in a careful and systematic fashion. As he distinctly states in the preface, "the book is intended to serve as a guide to the practitioner and student in the treatment of fractures of bone." The work is by no means an exhaustive discussion of the subject, but rather a clear, concise statement of the most important facts connected with each particular fracture together with a careful description of at least one satisfactory method of treatment of each fracture. A great effort toward simplicity in the treatment of fractures is evident throughout the book.

Especially to be commended are the illustrations in which the work abounds, and these are for the most part of a high degree of excellence. The results of careful studies of fractures with the X-rays are incorporated in many of the illustrations and afford abundant evidence of the value of skiagraphy in this department of surgery.

Chapters 1, 2 and 3 deal with fractures of the skull and vertebræ, fractures of the inferior maxilla receiving especial attention.

Chapters 4, 5 and 6 are devoted to fractures of the ribs, sternum and pelvis, with a brief reference to the urinary complications of fracture of the pelvis.

The next two chapters are devoted to fractures of the scapula and clavicle, while in chapters 9, 10 and 11 fractures of the arm and hand are carefully discussed, the portions devoted to fractures of the neck of the humerus and Colle's fracture being especially satisfactory.

Four chapters are devoted to fractures of the leg and foot, and in them, as well as in other parts of the book, the author illustrates the results of the treatment of fractures of the different bones by statistics from the Massachusetts General Hospital. The use of a general anæsthetic as an aid in the diagnosis and proper reduction of fractures is strongly advised.

Thrombosis, embolism and sepsis as complications of fractures are briefly discussed.

In considering gaseous phlegmon as a complication of fractures, the author speaks of the bacillus of malignant œdema as the causative agent and does not mention the bacillus *aërogenes capsulatus*.

Especially to be encouraged is the introduction by the author of the terms "closed" and "open" to replace the terms "simple" and "compound" as applied to fractures.

A brief chapter is devoted to the anatomy of the epiphyses and their importance in fractures.

A chapter written by Dr. Colman treats of the value of the X-rays in the diagnosis of fractures and briefly discusses the sources of error and the dangers associated with the use of the X-rays.

A short chapter is devoted to the employment of plaster of Paris in the treatment of fractures and methods of preparation of plaster of Paris dressings are described.

The book closes with a chapter on the ambulatory treatment of fractures with a brief description of the methods to be employed and the results that have been obtained.

Altogether this book shows great care and thought in its preparation, fulfils a decided need, and is one which can be recommended to both the student and the practitioner; it should receive the hearty endorsement of the profession.

A Text-Book of Pathology. By ALFRED STENGEL, M. D. Third edition. Revised. (*Philadelphia: W. B. Saunders & Co., 1900.*)

In this edition the author holds to his original purpose of supplying the clinician with a concise book on pathology, and he has briefly outlined the main points of general and special pathology within the limits of a text-book of moderate size. On account of the condensation necessary in a work of this kind, the book is hardly one that would be suitable for those beginning the study of pathology. It is a store-house of facts which are necessarily stated boldly and dogmatically. A greater diffuseness and amplitude of statement would add much to its value for the use of students. The volume is abundantly illustrated, and contains a full index which adds much to its value as a book for ready reference.

A Manual of the Diagnosis and Treatment of the Diseases of the Eye. By EDWARD JACKSON, A. M., M. D., Emeritus Professor of Diseases of the Eye in the Philadelphia Polyclinic, with 178 illustrations and 2 colored plates. (*Philadelphia: W. B. Saunders, 1900.*)

The book is all that it purports to be—a manual for students of ophthalmology and for the general practitioner of medicine—and we believe it serves its purpose admirably. It seems particularly well adapted to the wants of medical students, containing, as it does, such a distinct, clear-cut, conservative and concise exposition of ophthalmologic subjects. The bibliographic appendix to each chapter, giving references to the best articles published on the subject discussed therein, is a decidedly valuable feature of the book. It broadens the scope of the work very considerably without interfering much with its brevity.

To review each chapter in detail is unnecessary, indeed, the well known reputation of the author is sufficient guarantee of the character of the book and we heartily commend it to both students and physicians.

H. O. R.

Panama and the Sierras: A Doctor's Wander Days. By G. FRANK LYDSTON, M. D. Illustrated from the author's original photographs. (*Chicago: The Riverton Press, 1900.*)

This little book of nearly 300 pages is written in an easy, readable style, and contains much of special interest to the physician, although not in any sense a medical book. The writer has an excellent ability to describe what he sees, and he sees almost everything which passes about him. In some instances he is flippant, but he is always interesting. The book contains an account of a journey for health made to California by way of the Isthmus of Panama and the experiences of the writer upon the Isthmus, in Mexico, and also in California.

Dr. Lydston is a native of California, and in revisiting the State he renewed his acquaintance with many towns in the mining region with which he was familiar as a boy. The account which he gives of the exhausted mines and deserted mining settlements is most interesting. The illustrations are good, but some of them should have been spared a sensitive and susceptible reader.

Rhinology, Laryngology and Otology, and their Significance in General Medicine. By E. P. FRIEDRICH, M. D., Privatdocent at the University of Leipzig. Authorized translation from the German, edited by H. HOLBROOK CURTIS, M. D., Consulting Surgeon to the New York Nose and Throat Hospital and to the Diphtheria and Scarlet Fever Hospitals. (*Philadelphia: W. B. Saunders & Co., 1900.*)

In these days of extreme specialization in medicine, when many of the leaders in our profession are seriously considering the problems arising from the rapid growth of specialism and the tendency of specialists to ignore the interdependence of abnormal conditions of the general health and of the special organs, it is refreshing and encouraging to read such a book as Friedrich's, in which the preface opens with the statement that, "there is (at present) a laudable tendency to tighten the bonds that unite the daughters to the mother science." However much honor is due the individual worker who devotes his time and energy to the study of special parts of the body, or special diseases, the ideal physician, whether specialist or not, is, unquestionably, he who combines with his special knowledge a broad conception of general medicine. Rarely does one meet with a physician who unites these qualities in his personality to such an admirable degree as does Dr. Friedrich.

Throughout the entire book, the one thing that impresses the reader more than all others, perhaps, is that the author not only possesses a fairly complete knowledge of the specialties under consideration but is able at all times to view the conditions present from the standpoint of the general practitioner; never for a moment losing sight of the most minute detail in the constitutional disturbance.

The author's keen, conservative, impartial judgment in the consideration of all debatable points also impresses the reader. Evidence from all sides is set forth fairly and honestly weighed. When the facts seem to warrant it, a decision on the merits of the case is rendered but always in a spirit of full conservatism.

The first chapter is devoted to a very brief consideration of the anatomical relations existing between the nose, pharynx, larynx and ears, both with regard to continuity of surface and similarity of tissue structure, and to a study of the effects, general and local, of diseases of the respiratory tract. The significance of the upper air passages in the physiology of breathing is given special attention, much emphasis being laid upon the importance of the nose as the respiratory pathway.

Chapters 2, 3 and 4 deal with the alterations in the upper air passages and ears, that may be met with in the course of diseases of the circulatory and digestive systems and of the blood.

Chronic constitutional diseases like rachitis, acromegaly, diabetes and gout are considered in chapter 5. The conflicting theories regarding the etiology of laryngeal spasm and its connection with rachitis are reviewed and the conservative opinion offered that "the most we can say is that spasm of the glottis in children is the expression of an abnormal excitability of all the respiratory muscles, and that it often occurs, in association with tetanic symptoms, in rachitic subjects as the result of digestive disturbances." No one can object to that.

The next two chapters, devoted to the acute and chronic infectious diseases, deserve special mention, but nothing like a satisfactory review can be made in brief. Twenty-five pages are given to tuberculosis alone and are well worth reading. The important rôle played by measles, scarlatina, typhoid, diphtheria and influenza in the causation of suppurative otitis media is thoroughly discussed. In passing, we may mention that the otitis in measles is attributed to the appearance in

the aural mucous membrane of lesions exactly like those seen on the buccal and pharyngeal membranes, showing that it is a part of the general symptom complex and not due to extension of infection through the Eustachian tubes. In scarlatina the extension theory is again cast aside and evidence adduced to show that the aural complications are toxic in character; a parallel being drawn with scarlatinal nephritis.

Syphilis naturally comes in for a large amount of space in the chapter on the skin and sexual organs. The physiologic and pathologic relations between the upper air passages, especially the nose, and the organs of sex are considered and Dr. Mackenzie's article given special reference.

The last chapter is given to nervous diseases, and an appendix follows dealing with the cranial nerves and with the sequelæ of otorrhœa, with reference principally to involvement of the brain, meninges or sinuses.

The book is well printed on excellent paper and is creditable to publisher, author and translator alike. It is not intended for a text-book nor a treatise on special diseases or organs but, as its title implies, is a link to bind the specialist and general practitioner closer together. Its abundant references constitute it a valuable index to the literature of the subjects treated.

H. O. R.

An American Text-book of Physiology. Edited by WILLIAM H. HOWELL, Ph. D., M. D. Second edition, revised. Vol. I. (Philadelphia: W. B. Saunders & Co., 1900. Price, \$3 net.)

The "American Text-book of Physiology," the first volume of the second edition of which has just appeared, differs in several respects from the text-books of physiology in general use at present. In the first place it is written by a number of men who are investigators in physiology as well as teachers; many of the experiments described and figures and curves reproduced are from the writers' own researches. By the division of the work among a number of contributors, the literature of physiology has been examined first-hand and the results of the most recent investigators incorporated; too many of the text-books offered to students are mere compilations from older and larger works. The fact that the contributors are themselves working physiologists and have gone over the literature of their respective subjects in a critical manner gives the book a freshness and interest seldom found in an elementary text-book. The objection that the treatment of a subject will probably lack uniformity when there are several authors does not seem to have much weight as far as physiology is concerned; at least the want of uniformity in the various sections of this text-book is decidedly less noticeable than that found in most of the books written by individual authors. When the books of the latter class are examined it is found that in almost every case some part of the subject receives what most physiologists consider to be undue emphasis; the part thus treated varies according to the subjects in which the various authors happen to be chiefly interested. In the present case the writers, having comparatively small fields of physiology to cover, have been able to get a better grasp of their part in all its phases than is possible for a man who has the entire subject of physiology to discuss.

The first edition of this text-book, which was published four years ago, appeared in the form of a single volume of over a thousand pages; to many this volume seemed inconveniently large, so that in the present edition the work has been divided into two parts. In the first volume the physiology of the blood, circulation, secretion, digestion, nutrition, respiration and animal heat and the chemistry of the body are considered. The editor has written more than a third of this part, and it seems to the reviewer that this writer's contributions are deserving of

special praise; they are characterized by great clearness and accuracy of statement, and the most important points are kept in the foreground while isolated details of minor importance are avoided. In a brief introduction Professor Howell discusses the more general problems of physiology and the composition and general activities of living matter; then follow chapters by the same author on blood and lymph. Before the intricate problem of the formation of lymph is discussed a brief chapter on diffusion and osmosis and other physical processes, discussed from the standpoint of the newer physical chemistry, is introduced. The chapter on the mechanics of the circulation and the movement of the lymph is written by Professor Curtis, while the innervation of the heart and blood-vessels is discussed by Dr. Porter. Porter also contributes a section on the nutrition of the heart, a subject to the knowledge of which he and his pupils have made such important additions. The chapters on secretion, digestion and nutrition and the movements of the alimentary canal, bladder and ureter are written by Howell; the most noticeable feature of these chapters is the incorporation of the recent very valuable work of Pawlow on the relation of the nervous system to the secretion of the digestive glands and the full discussion of the subject of internal secretion. Respiration and animal heat are discussed by Professor Reichert, one of the few physiologists in this country who has had practical experience with the calorimeter. The final chapter of the first volume, on the chemistry of the animal body, is contributed by Professor Lusk; the recent work of Fischer on the purin bases and that of Kossel and his pupils on protamins are fully discussed.

In the second volume, which is to appear shortly, the physiology of muscle and nerve, of the central nervous system, of the sense organs and of reproduction will be discussed. The arrangement of the sections has been altered somewhat in the new edition; one change would seem to call for some comment. In the former edition the physiology of muscle and nerve was the subject first discussed; in the new edition this section is placed in the second volume "so as to bring it into its natural relations with the Physiology of the Central Nervous System." There are undoubtedly some advantages in this change, but it is questionable whether they are not outweighed by certain obvious disadvantages. With the present arrangement the reader meets constant references to the physiology of striped, plain and cardiac muscle, to nerve impulses, sympathetic nerve fibres, etc., before these elementary terms are defined—a manner of presenting the subject few teachers would care to adopt in their lectures.

On the whole this work is certainly the best text-book of physiology for medical students in the English language, and it will doubtless continue to be used generally in all medical schools of the first class.

R. H.

Modern Medicine. By JULIUS L. SALINGER, M. D., and FREDERICK J. KALTEYER, M. D., of Philadelphia. (Philadelphia: W. B. Saunders & Co., 1900.)

In this work of 800 pages the authors have endeavored to combine the essentials of physical diagnosis, bacteriology and clinical microscopy as applied to clinical medicine with the general description of diseases as usually taken up in a text-book of medicine. They state that "it has frequently been necessary for the student to procure separate books upon these topics." We hope that it will always be necessary for the student to do so. It is certainly advisable. The man who is studying medicine to-day and is not prepared to have a good text-book of medicine in addition to works on physical diagnosis and clinical methods had better choose some other calling.

In the first 100 pages general symptomatology and semeiology

re considered. This has necessarily been much condensed, but the authors have made the best use of the space. Clinical bacteriology occupies 22 pages, and then about 50 pages are given to laboratory methods. In the description of the methods of examination of the stomach contents no mention is made of Pöfner's test for free hydrochloric acid, nor is the question of ether extraction referred to in discussing Uffelmann's test for lactic acid.

The greater part of the book is taken up with the discussion of disease. Of necessity, the various diseases have to be considered briefly and only the most important points taken up. In the discussion of epidemic cerebrospinal meningitis no mention is made of lumbar puncture, our most valuable means of diagnosis. The writers have evidently been fortunate in their diagnosis of syphilis when they state that "it can scarcely be confounded with any other disease." They probably mean that the diagnosis of a typical case is easy, but it is such general statements, which of necessity have to be made, that constitute the great objection to books of this kind. There is something of everything, but not enough of anything.

Transactions of the American Surgical Association. Vol. XVIII. Edited by DE FOREST WILLARD, M. D., Ph. D., Recorder of the Association. (Philadelphia: Wm. J. Dornan, 1900. Cloth. pp. 468. Illustrated.)

This volume of the Transactions of the Surgical Association deals with subjects of much interest in modern surgery and the papers on the whole are of a high degree of merit. The symposium on gastric surgery quite thoroughly covers the subject of surgery of the stomach and contains papers of a great deal of value. The presidential address by Weir of New York embodies the result of much personal experience in the treatment of perforating ulcer of the duodenum and includes the abstracts of 51 cases which have been reported up to the present time. Godman of Philadelphia discusses hemorrhage from non-perforating gastric ulcer in a thorough manner and has carefully tabulated 40 cases which had been reported up to the time of publication of his paper. Finney discusses perforating gastric ulcer and tabulates the cases which have appeared during the past few months, bringing the subject up to date. Benign obstruction of the pylorus is discussed by Kammerer of New York; malignant disease of the stomach, by Mayo of Rochester, Minnesota; the surgical treatment of dilatation of the stomach, by Curtis of New York; the diagnosis of carcinoma of the stomach, by Hemmeter of Baltimore; and the surgical treatment of hourglass stomach, by Watson of Boston.

The volume also contains reports of some unusual and very interesting cases, including a case of stricture of the œsophagus following typhoid fever which was operated upon by gastrostomy by Dennis of New York; nephrectomy for a large aneurysm of the renal artery, by Keen; removal of acutely inflamed tuberculous mesenteric glands simulating appendicitis, by Richardson, and also by Elliott of Boston.

The present interest in the operative treatment of peritoneal infections in typhoid fever makes the paper by Warren reporting 27 cases of this kind of special interest.

The discussions on the various papers are given in full and contain much that is almost as valuable as the papers, many of which are among the most important contributions to the subjects under consideration which have thus far appeared.

Atlas and Epitome of Diseases caused by Accidents. By Dr. ED. GOLEBIEWSKI, of Berlin. Authorized translation from the German with editorial notes and additions by PEARCE BAILEY, M. D., Consulting Neurologist to St. Luke's Hospital and the Orthopedic Hospital, New York; Assistant in Neurology, Columbia University. 40 colored plates and 100 illus-

trations in black. pp. 549. (Philadelphia: W. B. Saunders & Co., 1900.) Price, \$4.

This book undertakes to give a systematic description of the sequels to injuries to all the organs of the body by accidents. It is divided into two parts, one treating of injuries in general, the other of injuries affecting the special structures and regions of the body. The book contains reports of numerous cases of injuries from various causes to illustrate the subjects under consideration, and a large number of fine colored illustrations. It is difficult to see the value of many of the illustrations, however. For example, it hardly seems necessary to devote a whole page cut to show the appearance of the scar resulting from a compound fracture of the femur and ilium or to show the appearance of the cicatrix following an operation in a case of strangulated hernia. Most of the illustrations seem to be of about this character. The text often seems very inadequate and inaccurate; for example, under hernia, we are told that "the external protrusion of any part of the intestine out of the abdominal cavity or its escape into another body cavity is called a hernia," without any reference to the possibility of omental hernia, hernia of the bladder and of other organs. Very much of the text will have little value for most physicians. The following is an example: "Incised wounds are produced by pieces of glass, sharp pieces of tin, by knives, saws, pieces of slate, etc. The greatest possible variety of wounds of the forearm is met with in workmen employed in the various trades and manufactures." Considerable space is devoted to a discussion of the length of time usually required for recovery from various injuries, the amount of loss of function and the allowance of insurance. Indeed, the book seems to be designed chiefly for German readers, the need of such a text-book arising from the law in Germany insuring all workmen against injury. Although the book contains reports of many interesting cases, we believe it will hardly prove of great value to the average American reader.

Elements of Clinical Bacteriology for Physicians and Students. By Drs. E. LEVY and F. KLEMPERER. Second edition, translated by Dr. AUG. A. ESHNER. (Philadelphia: W. B. Saunders & Co., 1900.)

This book, originally published in Germany and presented in English to the profession and students of America in a clear and comprehensible manner, is well classified and written, and contains numerous illustrations of an excellent kind.

Compared with many books of like nature in use in this country, it cannot be said to be their peer. And judged by the most recent American standards, its presentation of many technical details is found in some degree to be lacking in accuracy and compass. Nevertheless, a perusal of its pages will reveal interesting matter, such as the articles on botulism, the mycoses and disinfection.

N. MACL. II.

Saunders Pocket Medical Formulary, with an Appendix containing posological table; formulæ and doses for hypodermic medication; poisons and their antidotes; diameters of the female pelvis and foetal head; obstetrical table; diet list for various diseases; materials and drugs used in antiseptic surgery; treatment of asphyxia from drowning; surgical remembrancer; tables of incompatibles; eruptive fevers; weights and measures, etc. By WILLIAM M. POWELL, M. D. Sixth edition, thoroughly revised. (Philadelphia: W. B. Saunders & Co., 1900.)

The object of this neatly printed and attractive book is so well set forth in the title that little comment is necessary. It does not seem so much a formulary as a remembrancer, and it will be mainly useful as bringing to mind procedures and remedies which in the strenuous life of the busy practitioner are sometimes overlooked. It is well arranged for easy reference.

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BY E. R. LE COUNT, M. D.,

Assistant Professor of Pathology, Rush Medical College.

(From the Pathological Laboratory of Rush Medical College.)

Among theoretical conceptions of pathological processes to which disease is attributable are certain ideas that have at their inception the distinctness of a silhouette. With the advancement of knowledge, the margins of certain notions lose their definiteness and we find various processes uniting insensibly at their boundaries. The idea that necrosis means death of tissue remains firmly planted, but the exact limitation of its import is considerably blurred when the process of gradual death is screened behind the caption of atrophy. Any attempt deserves approval that

has for its object the segregation and classification of morbid processes that lie in the boundary zone. It seems, however, that as time advances the narrow distance now separating the process of tissue hyperplasia from that concerned in the development of benign tumors will not be increased. Lubarsch,¹ after commenting on the close connection between tumors and infectious processes, notes this difficulty in the following words: "Suchte man daher nach anderen un-

¹ Ergebnisse d. allg. Path. u. path. Anat., 1895, ii, p. 290, Wiesbaden.

terschiedenen Kriterien, so machte sich eine weitere Schwierigkeit, die Abgrenzung gegenüber die Hyperplasie bemerkbar." Still, it is evident that if a process of questionable character midway between tumor and hyperplasia can be traced to an inflammatory origin, its position is no longer in doubt. It must of necessity be considered as hyperplasia or the meaning of the word tumor will require modification. In lesions of such uncertain species, in which the inflammatory origin is manifested by simply one of the inflammatory phenomena, viz., that of proliferation, the question seems surmountable in only one way—to admit without further discussion the existence of a firm bond uniting them. Such a solution of the problem is rendered easy by finding lesions which represent all transition stages from one process to another. An example of this kind is reported by W. W. Van Arsdale:² a growth developed on the upper right arm two days after several blows received during a sparring bout. A fluctuating swelling that increased the circumference of the arm 10 cm. was present two days after injury; one month later the mass had decreased to one-third its former size, but it had become hard and immovable. Two months after the injury, a growth 9 cm. in length and 3 cm. in its other diameters was chiseled from between the biceps and branchialis anticus; it was found to possess an outer shell of bone 1.5 cm. thick, the periosteum being closely adherent to its exterior, and a cavity filled with dark partially coagulated blood; its outer wall was true bone and its cavity devoid of bone-marrow proper; its inner wall was porous vascular bone.

It seems reasonably certain that in this case the clot of a subperiosteal hemorrhage became ossified at least in its outer part. According to Klebs,³ the process of bone-formation in this "Ossifying hematoma" would serve as an example of hyperplasia; for, he states, the line between hyperplasia and tumor-growth may be determined to some extent by the preponderance of the former in scars and granulation tissue and its proneness to spontaneously disappear. The growth would be inflammatory in origin, for the unabsorbed blood would excite an inflammation in the surrounding parts (Cohnheim).⁴ According to Lubarsch,⁵ the apparently autonomous hyperplastic growths almost without exception follow inflammatory excitants. Notwithstanding these opinions, it is unreasonable to suppose that had ossification been allowed to continue throughout the entire coagulum, that the mass of new bone would ever have disappeared spontaneously; there would have resulted an osteoma—a benign tumor. Surgeons are well acquainted with the permanent character of the bony hyperplasia which occurs in a luxuriant callus and the osteomas that develop in the biceps and pectoral muscles from the kick of a gun (Tillmanns).

Another instance of lesions which represent transitions between hyperplasia and benign tumor is furnished by mul-

tiple adenomata of the liver. In proof of their mediate position is the fact that equally good authorities are arranged on opposite sides: Weichselbaum, Rindfleisch, Chiari and Kretz classify the condition with simple hyperplasia; Lubarsch, Thoma, Ponfick and Eppinger with adenomata. Orth⁶ seriously considers the question of tumors arising from multiple nodular hyperplasia of the liver, and Schmieden,⁷ in a recent review of the connection which exists between these lesions, declares that a sharp division between adenoma and hyperplasia in the liver cannot be made. He claims to have seen, as Van Henkelon did before him, the transition forms between hypertrophied liver cells and tumor cells. The relationship between hyperplastic processes and tumor is more important when it has to do with cells that possess great powers to proliferate and regenerate, *e. g.*, surface epithelium and the epithelium of superficial glands. In discussing this subject Birch-Hirschfeld⁸ makes the statement that such atypical hyperplastic growths show in the excess of their regeneration certain points of similarity to tumors, and it may be accepted that they may become changed into tumors; he also states⁹ that the possible occurrence of growths which represent transition stages between hyperplasia and tumor can not be excluded.

The effect of a productive inflammation or inflammatory hyperplasia upon mucous linings is either a diffuse and uniform thickening or the formation of the isolated polypoid outgrowths. As the gross appearances change from a diffuse process to dispersed or widely scattered growths, the likelihood of the inflammatory origin lessens, for the conception of a tumor is connected with the local limitation of its early growth (Thoma). But to this there are exceptions, for "the inflammatory new growths, which are due to atypical proliferation of epithelium, tend to form either single, tumor-like protuberant growths or multiple growths over a considerable surface" (Birch-Hirschfeld).

The confusion which attends the word papilloma is no more attributable to its diversity of structure than to the question of its proper position in regard to tumors and the hyperplastic inflammations. Birch-Hirschfeld¹⁰ states that in mucous membranes a diffuse or circumscribed polypoid thickening may result from chronic catarrhal inflammation; also, that in the nose¹¹ combinations of papilloma and hyperplasia of the mucosa occur. Klebs¹² uses the polypi of the stomach to illustrate the effect of hyperplastic inflammation in the production of papilloma. In the statement by Orth¹³ concerning the papillomata of the Fallopian tube, that it is difficult to determine with certainty to what extent they are caused by inflammatory growths of the folds of the mucosa, we have further evidence of the confusion.

² Ann. Surg., 1893, xviii, p. 8, Phil.

³ Die allg. Pathologie, etc., ii, p. 491, 1889, Jena.

⁴ Vorlesungen über allg. Pathologie, p. 393, 1882, Berl.

⁵ L. e., p. 297.

⁶ Lehrbuch der spec. path. Anatomie, i, p. 957, 1897, Berl.

⁷ Arch. f. path. Anat. (etc.), elix, p. 290, 1900, Berl.

⁸ Grundriss der allg. Pathologie, p. 144, 1892, Leipzig.

⁹ Lehrbuch der path. Anat., i, p. 180, 1896, Leipzig.

¹⁰ L. e., p. 137.

¹¹ Lehrbuch der path. Anat., ii, p. 450, 1894, Leipzig.

¹² L. e., p. 615.

¹³ Lehrbuch der spec. path. Anat., ii, p. 539, 1889, Berl.

Such uncertainty of classification leads naturally to the use of terms which are devised to bridge over the difficulty. Such a title, alluding both to the process of hyperplasia and to the admixture with tumor, is used by Hauser¹⁴ in his report of a case of "Polyposis intestinalis adenomatosa." In this case there were disseminated polypi consisting largely of atypical epithelial growths not only throughout the intestinal canal but also in the stomach. Hauser refers to three other similar cases. Petrow¹⁵ has added another in which there were numerous single or clustered, large and small polypous growths in the stomach and the entire intestinal canal, together with every evidence of a severe chronic inflammation in the mucous coats involved.

Quénu and Landel¹⁶ have recently collected 42 cases in which the large intestine was the seat of a more or less extensive polypous hyperplasia. From the frequent history of diarrhoea, these authors believe that the process has its origin in inflammatory conditions, and this opinion is reached after a thoughtful consideration of the possibility that the intestinal disturbances might be secondary to the multiple adenomata. In a previous article by the same authors¹⁷ there is even less doubt displayed respecting the identity of pedunculated adenomata of the rectum with hyperplastic processes, for the statement is made that "they are more or less directly dependent upon an inflammatory reaction."

Sklifossowsky,¹⁸ after describing two benign papillary tumors in the mucous lining of the stomach, states that they originated from a hyperplasia of the mucous coat due to long-standing irritation; he likens them to the knob-like projections of the *état mamelonné*. His interest in these growths was largely due to the fact that all transitions were found in them between the diffuse thickening of gastritis proliferans and the tumors described.

Further evidence is not necessary to illustrate the fact that hyperplastic processes in the mucous lining of the gastro-intestinal tract, like those of the liver, are closely allied to the processes of tumor-development; or that there are certain interposed lesions which might be accepted as proof of the continuity of processes having as their onset chronic inflammation, and, as their termination, tumor-growth. The analogy will be more complete with the demonstration of cases such as are hinted at by Birch-Hirschfeld¹⁹ in the following proposition: "It is probable, but not proven, that certain forms of primary carcinoma of the liver may have their origin in a further atypical development of such liver adenomata." The fact that the hyperplasia of the gastro-intestinal mucosa has, as its end product, the

evolution of *malignant* neoplasms, leaves no room for controversy such as has been noted with regard to multiple adenomata and nodular hyperplasia of the liver.

In 42 cases gathered by Quénu and Landel of polypous hyperplasia of the colon, there were 20 in which a carcinoma of the colon was also present. In the series of Hauser,²⁰ of carcinoma of the colon, five were associated with more or less extensive "polyposis," and in the stomach the same author reports one case in which the process was combined. (Case 25, p. 208.)

One of the cases of benign tumor of the gastric mucosa which Sklifossowsky so positively ranks with the inflammatory hyperplasias, possessed at the same time a carcinoma, which was sufficiently interesting, on account of the early changes it showed, for Israel to report it under the title "Ueber die ersten Anfänge des Magenkrebs." ²¹ Also, in the case of Petrow, of diffuse gastro-intestinal polypous hyperplasia, death took place from invagination and spontaneous rupture at two places, where the growth had a similarity to adenocarcinoma.

To substantiate the view that the polypous growth occurs first and that the production of tumor follows, the following citations will suffice:

Orth,²² in considering similar growths in the Fallopian tube, writes as follows: "Among the recently reported cases of papillary new growths are some which may be correctly deemed benign and others which are malignant; from the great similarity of these to one another it is safe to accept the view that there is at least a danger of cancerous transformation. Hauser, in the report mentioned of a case of Polyposis intestinalis adenomatosa, claims (p. 446) that one must admit that the multiple warty growths have developed first and that these later underwent a carcinomatous change. Cullen,²³ after referring to the opinion of Lubarsch, that a benign tumor is never changed into a malignant one, says:

"Case 4,262, which I have recently had the opportunity of studying, shows beyond a doubt that such a possibility exists." The case in question was that of a polypous adenoma of the uterine mucosa.

The investigations on inflammatory hyperplasia with tumor-formation in certain regions have been repeated by Stoerk²⁴ in the urinary tract. He describes a case of papillomatosis of the urinary bladder, ureter and pelvis, of the right kidney, and was able to find only two similar cases in the literature. He considers the process as an unusual form of chronic inflammatory hyperplasia, and compares it with Gastritis proliferans. More commonly the chronic inflammation in the urinary passages terminates in a hyperplasia associated with the formation of cysts. That certain cases should display both features of the process is not sur-

¹⁴ Deutsches Arch. f. klin. Med., lv, p. 429, 1895, Leipzig.

¹⁵ Bolnitsch. gas. Botkina, 1896, St. Petersburg. From the summary of Russian literature by Maximow and Korowin, Ergebnisse d. allg. Path. u. path. Anat., Lubarsch and Ostertag, v, p. 735, 1898, Wiesbaden.

¹⁶ Les polyadénomes du gros intestine. Rev. de Chir., xix, p. 465, 1899, Paris.

¹⁷ Rev. de gynéc. et de chir. abd., ii, p. 484, 1898, Paris.

¹⁸ Arch. f. path. Anat. (etc.), cliii, p. 130, 1898, Berl.

¹⁹ L. c., p. 743.

²⁰ Das Cylinderepithel-carcinom des Magens und des Dickdarms, p. 261, 1890, Jena.

²¹ Berl. klin. Wchnschr., xxvii, p. 649, 1890.

²² L. c., p. 539.

²³ Cancer of the Uterus, etc., p. 355, 1900, N. Y.

²⁴ Beitr. z. path. Anat. u. z. allg. Path., xxvi, p. 367, 1899, Jena.

prising. Litten²⁵ has described "Ureteritis chronica cystica polyposa." Cahen²⁶ has one case, and to this Stoerk adds three more, in which the hyperplasia of the mucous lining of the bladder was accompanied by carcinoma. Rehn²⁷ makes the interesting statement that in the majority of tumors of the bladder a substance in solution in the urine causes the tumor-growth by its chemical irritation; he has observed three cases in which tumors of the bladder occurred in men employed in the manufacture of aniline dyes. Stoerk is inclined to lay strong emphasis upon gonorrhœa as an etiological factor, and Kaufmann²⁸ has described the occurrence of multiple polypi in the ureter from the passage through it of feces from a fistulous connection between the pelvis of the kidney and the duodenum. As an example of the question which so constantly recurs—tumor or inflammation—and serving as an illustration of the apparent necessity to separate these conditions, the following quotation will answer:²⁹ "The condition described might be classed both as chronic cystitis and as tumor. . . . I am inclined to look upon the process as a chronic cystitis." This is in concluding an article on Cystitis Papillomatosa, where the cystoscopic examination left the observer in doubt. In the recent work by Cullen on Cancer of the Uterus, there is abundant evidence that a diffuse polypous hyperplasia of the uterine mucosa occurs and that this condition may be combined with carcinoma. The illustrations on pages 514 and 516 show its gross anatomy; some participation of the epithelium in the process is evident, since in many places it was many layers in depth in both cases, notwithstanding that no karyokinetic figures were found. Case 3,452 (p. 323) of "adenocarcinoma of the anterior cervical lip; commencing adenocarcinoma of the posterior lip, apparently independent of the former; papillary outgrowths of the uterine mucosa, with suspicion of commencing adenocarcinoma of the body of the uterus," is a striking analogy with the polypous hyperplasia with carcinomatous transformation observed in the intestinal mucosa and the urinary tract. Perhaps the best example of polypos hyperplasia described by Cullen is Case 6,659 (p. 401). Occurring in a young woman, aged 30, this author describes "a very unusual polypoid condition," in which "the mucosa, as a whole, presents a most unusual picture, consisting of large polyp-like masses springing from all parts and completely filling the enlarged cavity." Histologically, "one of the chief features is the preservation of the lumina of the glands; few, if any, nuclear figures are to be made out," and "the uterine muscle has not been penetrated by the growth; in fact, at some points there still remains a small amount of normal mucosa separating the growth from the muscle." There had been no recurrence of tumor 11 months after the removal of the uterus. The diagnosis was adenocarcinoma. There is but little doubt,

so far as one can judge from the report, that in this case the process was one of diffuse polypous hyperplasia which, so far as the examination shows, had not at the time of removal undergone carcinomatous change. That such a change would have occurred, had it been undisturbed, might be inferred from the continuity of process which has been shown so far to exist between the polypous hyperplasia and carcinoma.

But it is especially concerning tumors of the Fallopian tube that confusion has arisen; there has been quite a general failure to recognize that a diffuse hyperplastic inflammation is possible—a process which is strictly analogous to the polypos hyperplasia of other mucous surfaces—and that in certain typical examples it is as distinct from tumor-growth as gastritis proliferans is from carcinoma of the stomach. Part of the confusion is no doubt due to the fact that hyperplasia is so frequently combined with sacto-salpinx. Slavyanski³⁰ has recognized this fact, as is established by the frequency with which he uses the term *sacto-salpinx papillomatosa*, although he does not clearly distinguish between papilloma as a tumor and polypous hyperplasia due to chronic inflammation. He states that "with occlusion of the abdominal end, the tube appears larger, aside from the papilloma; products of the secretion both from the covering of the tumor and the diseased mucosa accumulate in the tube; thus sacto-salpinx becomes sacto-salpinx papillomatosa (p. 112)." Numerous investigations in lower animals have proven that when the outer end of the tube is closed a retention cyst is the result.³¹ Undoubtedly in many cases the inflammatory process which leads to the hyperplasia of the mucous lining of the tube causes the closure of the abdominal end. As a typical example, the case reported by Doléris and Macrez³² will answer. He removed from a woman, aged 37, a growth of the right tube which was adherent to the liver and measured 20 by 30 cm. It consisted of a sac filled with grumous, viscid, yellowish fluid; its walls were 5 to 10 mm. and the lining was beset with pin-head to pea-sized papillary growths, which, on microscopic examination, consisted of villi with rarely more than one layer of epithelial cells as a covering. This is the second growth of this sort removed by Doléris; the other, in 1891,³³ being the first observed in France. The woman was 28 years old; the growth was in the right tube and the inner one-fourth of the sacto-salpinx contained no papillary growths. Clark has reported a similar case³⁴ of a cystic growth of the Fallopian tube 12 by 12 cm., or one-half the size of a man's head, in which the inner surface was studded with thick papillary growths except at one point, where the

²⁵ Arch. f. path. Anat. (etc.), lxi, p. 139, 1876, Berl.

²⁶ Arch. f. path. Anat. (etc.), cxiii p. 468, 1888, Berl.

²⁷ Verhandl. d. deutsch. Gesellsch. f. Chir., xxiv, s. 240, 1895, Berl.

²⁸ Cited by Stoerk.

²⁹ F. Bierhoff, The Medical News, lxxvi, p. 810, 1900, Phil.

³⁰ Special Pathology and Therapy of the Diseases of Women, vol. ii, Diseases of the Fallopian Tubes and Ovaries (Russian), 1897, St. Petersburg.

³¹ C. Gebhard: Pathologische Anatomie der weiblichen Sexualorgane, pp. 436-7, 1899, Leipzig; also: Ergebnisse d. allg. Path. u. path. Anat., 1898, v, 741 (work of Sadkowsky), Wiesbaden.

³² La Gynecologie, iii, p. 289, 1898, Paris.

³³ Nouv. Archiv. d'Obstet. et de Gynec., vi, p. 11, 1891, Paris.

³⁴ Johns Hopkins Hospital Bulletin, ix, p. 163, 1898.

surface for an area the size of a palm was smooth. The wall of this cyst was thin; the warty growths were largely made up of connective tissue, and the epithelial covering of these was uniformly single-layered. Although Clark ascribes the process to inflammation, it is reported as the seventh instance of papilloma of the Fallopian tube. Another instance first reported on account of the concurrent appendicitis³⁵ was shown on later examination of the sac,³⁶ which was as large as a foetal head, to contain the inner part of the tube as a curved cord on its outer surface. The lining of the sac was beset with small growths covered with epithelium; the crypts between the growths extended outward so as to give to the section an appearance not unlike an adenoma. The condition described in this case might be considered as analogous to cystitis cystica of Stoerk and others, which led Aschoff to search for glands in the urinary tracts of newly born infants. It is essentially the same process—a hyperplasia of the lining (sacto-salpinx villosa et pseudo-follicularis). Both this case and that of Montprofit and Pilliet³⁷ are included by Macrez in the table of benign papillary tumors of the tube; in concluding the case above mentioned, the following interesting statement is made:

“L'origine irritative de ces productions dans la trompe ne doit pas surprendre, puisque l'on voit que dans les viscères comme le foie, le rein, la capsule surrénale, etc., les formations adénomateuses coexistent avec la sclérose et paraissent être un des modes de réaction des cellules parenchymateuses aux irritations qui amènent l'épaississement du tissu conjonctive.”

The second case of papilloma reported by Doran³⁸ was double-sided; the right tube contained over a pint of fluid, the left a smaller amount. Both contained papillary growths which Doran describes as warts “similar in principle to those found in other structures, namely, overgrown papillæ, the result of continued irritation.”

It is certainly of doubtful propriety to consider these growths, so clearly the products of an inflammatory action, as “papilloma.” Sacto-salpinx papillomatosa might be altered with advantage to Sacto-salpinx polyposa, for the condition is one of diffuse polypous hyperplasia associated with the formation of a retention cyst and not one of tumor-growth. By some observers the diffuse villous hyperplasia associated with sacto-salpinx has been reported as carcinoma. W. L. Jakobson³⁹ has reported a case in which the papillary growths almost filled the sac. Although the epithelium had not proliferated so as to invade the musculature of the tube, and notwithstanding that there were no metastatic growths, the condition of the tube was diagnosed carcinoma by both Jakobson and Petroff, who made the histological examination. In the case reported by Hofbauer⁴⁰ both tubes were

closed externally, but retention cysts were absent. The lining of the right tube, in which the changes were more advanced, possessed small miliary and larger growths, some as large as two beans. From the gross changes and from the careful description of the histologic structure, this might also be considered as polypous salpingitis, did not the record point so well to tuberculous salpingitis. The sac in the case operated by Leopold and described by Fearne⁴¹ measured 5 cm. in diameter and occupied the infundibulum and ampulla of the tube. It was filled with a soft vascular papillary growth. The lining folds have hypertrophied, branched, and then, according to Fearne, undergone malignant transformation. The muscle fibers had disappeared by atrophy and a firm connective-tissue wall had so successfully limited the process that there were no metastatic growths and the patient was well 1½ years later.⁴² The case reported by Säger and Barth,⁴³ over which they hesitated long before concluding that it was one of carcinoma, which diagnosis has constituted one of the principal factors of the present confusion, was one in which the tubal mucosa was thickened so that it resembled the cerebral convolutions in miniature. The accompanying illustration, showing the macroscopic appearance of the lining, resembles greatly the mammillated appearance of the stomach in gastritis proliferans. This thickening affected the outer one-half of the tube uniformly; there were numerous nuclear figures in the epithelial cells which covered the villi in a single layer, and largely from this histologic similarity with “Adenoma malignum” of Ruge and Veit, these authors concluded finally that it also was carcinoma. The diffuse character of the process in this case, and the uniformity with which the tubal mucosa was involved, point to a hyperplasia similar to that seen in other mucous coats—to a condition resulting from inflammatory reaction with excessive proliferation or the early disappearance of all other changes but proliferation—a process which Adami, following Klebs, refers to as “neoplastic hyperplasia,” and which Hauser, as before noted, connects with tumors by the term “polyposis adenomatosa.”

It does not always happen that the outer end of the tube becomes closed by the inflammatory process; the subsequent invasion of the adjacent peritoneum, by papillary or warty growths, however, is no proof that the process is one of tumor-growth; for, in condyloma acuminata an exactly similar process occurs—extension of a hyperplastic inflammation by direct continuity of surface. The classical case of Doran⁴⁴ is of this nature. The outer part of the right tube was dilated and filled with cauliflower-like growths; these were formed by villi covered by a single layer of epithelium of which some cells were ciliated. There was also an enormous ascites and pleural effusions which required frequent

³⁵ Bull. Soc. Anat. de Par., 1897, xi, n. s., p. 518.

³⁶ P. Macrez: Des Tumeurs papillaires de la Trompe de Fallope, p. 61, 1899, Paris.

³⁷ Bull. Soc. Anat. de Par., 1893, vii, p. 505.

³⁸ Tr. Path. Soc., 1888, xxxix, p. 200, London.

³⁹ J. akush. i jensk. boliez., xii, p. 29, 1898, St. Petersburg.

⁴⁰ Arch. f. Gynäk., lv, p. 316, 1898, Berl.

⁴¹ Über primäre Tubencarcinom. Geburtshilfe u. Gynäkologie, ii, p. 337, 1895, Leipzig.

⁴² Tr. Obstet. Soc. (London), 1898, xl, p. 202.

⁴³ Die Krankheiten der Eileiter, A. Martin, p. 253, 1895. Berl.

⁴⁴ Tr. Path. Soc. (London), 1880, xxxi, p. 174; Idem., 1882, xxxiii Supplementary Reports, p. 49.

tapping; although it was impossible to remove the entire growth, no recurrence had taken place 16 years after the operation.⁴⁵ It is more reasonable to believe this case to be one of hyperplastic salpingitis than of tumor. Doran, in his original report, likened it to the venereal condylomas and to the inflammatory polypi of the tubal mucosa described by Rokitansky and Hennig.

Another condition has been described by Schirschoff⁴⁶ as papilloma. It is that of a single pedunculated tumor which arose from the lining of the tube 5 mm. inside the fimbriæ; the abdominal os was wide and gaping. The growth was 5 cm. in length and made up of a cluster of smaller masses. The exact pathologic position this growth should occupy as regards the Fallopian tube will always be in doubt, since there is but slight mention of the large (wt. 410 g.) papillary cystoma which was situated just below the outer end of the tube. In other cases such localized growths have been catalogued as carcinoma. Stroganoff⁴⁷ has described a single pedunculated growth which arose from the mucosa by a pedicle 1 cm. in diameter. The tube containing it was closed externally and held about 50 cm. of the usual sero-hemorrhagic fluid. The structure of this growth was such that a diagnosis was made of "carcinoma cylindro cellulare." There is no mention of regional invasion, glandular involvement or recurrence; the woman was 39 years old. Tuffier⁴⁸ found in a tube, which was closed externally, pear-shaped and as large as a foetal head, a dark, soft and friable mass which was at first supposed to be free; in examining it a narrow pedicle was found. The lining of the sac containing this growth was, for the greater part, smooth and devoid of epithelium. The examination of this growth alone, which, like that of Stroganoff, was largely necrotic, led to a diagnosis of carcinoma (epithelioma).

Falk⁴⁹ also described a localized growth as carcinoma. On the left side the tube formed a sac that contained a sanious, semi-purulent fluid and in its outer part gelatinous cysts; the sac formed by the right tube was as large as a child's head. It contained a similar fluid, free, grayish, villous masses, and on the posterior wall springing from the mucosa, a growth the size of a walnut; this contained gland-like structures, and from its histologic resemblance to the case of Sänger and Barth, a diagnosis of carcinoma was reached. It is obvious that in this instance the chronic inflammation on one side caused sacto-salpinx with hyperplasia of the lining and the formation of pseudocysts; on the opposite side, sacto-salpinx with the production of a localized growth. In cases of this nature, the effort to separate tumor and hyperplasia meets, in the localized nature of the growth, an obstacle which is at present insuperable. If there occur in

such localized growths evidences of the multiplication of cells—nuclear figures—or if alterations are found in the morphology and staining reactions of the cells which would indicate that they have not reached an adult type, the process is certainly more like tumor than like hyperplasia. But between hyperplasia and carcinoma there is a considerable gap. Hauser, after describing the multiplication of the glands in the polypi of the intestine, makes the statement⁵⁰ that it should not be understood that all such growths are of necessity precursors of carcinoma. With the article of Schmieden⁵¹ there are portrayed atypical karyokinetic figures in the liver cells which form the adenomata. In short, it seems to me that the case described by Falk does not correspond to carcinoma so much as it does to a benign and localized growth; here it is necessary to recur to a proposition made earlier—that it is doubtful whether the narrow distance now separating hyperplasia from benign tumor will be increased. It is reasonable to believe that there should occur in the lining of the Fallopian tube regenerative processes, similar to those of glandular organs and structures possessing glands, the products of which are closely allied to adenomata.

The foregoing considerations demonstrate the imperceptible transition of hyperplastic processes of the tubal mucosa—belonging properly to the salpingitides—into those of true tumor growth; and that these may terminate in the production of benign tumors. The literature of tubal tumors also contains abundant evidence that the transition of villous hyperplasia into growths that at least possess some indications of malignancy is an equally gradual one. The tumors demonstrated by Kaltenbach as double-sided tubal carcinoma⁵² were later elaborately described as papillomata.⁵³ Carcinoma is positively excluded in the following words: "Aber nirgends lässt sich doch ein Anhaltspunkt für eine wirkliche Carcinombildung finden, auch da nicht, wo die Neubildung mehr einen parenchymatösen Character hat, und von einer Zerstörung des bindegewebigen Papillärkörpers durch eingedrungene Epithelmassen ist nichts zu sehen." Notwithstanding this statement, there was a recurrence within 18 months.⁵⁴ In Eckhardt's⁵⁵ case the cyst formed by the dilated outer portion of the tube had small elevations on its external surface which, on microscopic examination, were found to consist of solid outgrowths of epithelium. In a report by Fabricius,⁵⁶ the left tube was removed and the growth that it contained pronounced papilloma by Paltauf. The right adnexa appeared normal and were left in place. Five months later a large growth occupied the right side of the pelvis, and masses removed from where the left tube had been amputated were declared by Paltauf to be carci-

⁴⁵ A System of Gynecology, by many writers, edited by T. C. Allbutt and W. S. Playfair: Diseases of the Fallopian Tube by Alban Doran, p. 806, 1897, London.

⁴⁶ Bolnitsch. gas. Botkina., Nos. 42-44, 1898.

⁴⁷ Collection of works in Obstetrics and Gynecology, dedicated to Prof. K. F. Slavyanski (Russian), p. 227, 1894, St. Petersburg.

⁴⁸ Ann. de Gynéc. et d'Obst., 1894, xlii, p. 203, Paris.

⁴⁹ Berl. klin. Wehnsch., 1898, xxxv, p. 554.

⁵⁰ L. e., p. 447.

⁵¹ L. c.

⁵² Centralbl. f. Gynäk., xvi, p. 357, 1889.

⁵³ Ztsch. f. Geburtsh. u. Gynäk., 1889, xvi, p. 364, Stuttg.

⁵⁴ Doran Tr. Obstet. Soc., 1898, xl, p. 200.

⁵⁵ Archiv f. Gynäk., 1897, liii, p. 183, Berl.

⁵⁶ Wien. klin. Wehnsch., 1899, xii, p. 1230.

noma. In the instance chronicled by Michnoff,⁵⁷ the folds of the lining of the left tube were thickened by many strata of epithelium and the muscular layers in some places were invaded through their entire thickness. The condition in the right tube considered by Michnoff as papilloma corresponds very well with saeto-salpinx villosa; the epithelium, rarely more than a single layer, covered papillary growths 1 cm. tall, and these filled the canal near the outer end of the tube; the os abdominale was closed and a cyst had formed there the size of a small hen's egg. In a case reported by Kretz as papilloma,⁵⁸ sacs had formed on both sides that exhibited externally small, white, soft, flat nodules. By the study of serial sections, these were found to be produced by the growth outward of the crypts between villi; the diverticula produced in this manner usually possessed a single layer of tall epithelium; where the epithelium was in two or three layers the cells were shorter and nuclei more spherical. Such cystic formations were found within the lymph channels.

Although it is not within the scope of this article to insist on the glandular character of the epithelial tubal tumors, certain facts may be pointed out. It is obvious that the five cases above cited as examples of growths that were removed during the transition between hyperplasia and tumor are very similar to proliferating papillary cystoma of the ovary. This similarity with ovarian tumors has been dwelt upon by many writers. Gebhard⁵⁹ compares them with uterine carcinoma in the following words: "Obwohl ich selbst, wie eingangs erwähnt, keine eigene Erfahrungen über das Tubencarcinom besitze, so bin ich doch bei der Durchsicht der in der Litteratur niedergelegten Beschreibungen des mikroskopischen Verhaltens dieser Geschwulst zur Überzeugung gekommen, dass dieselbe histologisch durchaus mit dem malignen Adenom u. Adenocarcinom des Uteruskörpers auf eine Stufe zu stellen ist."

The classification of tubal carcinomata into purely papillary and papillo-alveolar by Sänger and Barth⁶⁰ is but a makeshift for adenocarcinoma; as Cullen says,⁶¹ concerning adenocarcinoma of the uterus, "I am strongly of the opinion that where the papillary arrangement is most marked, the growth has started in the surface epithelium; whereas it seems probable that when the gland-like arrangement is more pronounced, the process has started first in the glands. The simpler plan would be to consider all these merely as variations in one disease." Slavyanski⁶² would limit the term adenocarcinoma to the latter form of Sänger and Barth. He separates them into two forms—carcinoma papillomatosa villosum and carcinoma cylindrocellulare seu adenocarcinoma.

From the description of the following case it may be seen that the view of Cullen relative to the two methods of growth in the adenocarcinoma of the uterus is equally applicable to

tubal carcinomata; that there is a disposition to grow towards the lumen in the form of branching villi as well as outward into the muscular coat as sacs, diverticula or alveoli, and that these methods of growth are part of the same process.⁶³

I received, June 22, 1899, from Dr. Henry P. Newman of Chicago, a tumor which was removed by him at the West Side Hospital. I am deeply indebted to him for the opportunity to examine it. The following abstract of the clinical history was also obtained from him:

Mrs. F., age 47, admitted to the West Side Hospital June 20th; in her early married life she had two miscarriages at the third and fourth months of pregnancy respectively. Subsequently, she gave birth at term to a child, which is now 21 years of age; delivery was instrumental and severe. Since then she has been unable to carry a child beyond the third or fourth month of pregnancy. In spite of many miscarriages she has enjoyed a fair degree of health until two years ago, when menstruation became painful. The pain was referred to the sides and lower abdomen; it began just before the flow and continued during the entire period; there was also experienced general weakness and exhaustion on slight exertion. One year ago she first noticed a protrusion from the vagina which she took to be the womb; this has gradually enlarged, becoming more prominent after standing, straining, and coughing. It has never been painful, but has proved annoying in walking or sitting from its large size. There has also been an enlargement of the abdomen until it is now as large as a pregnancy at full term. She complains of a frontal headache; she has a fair digestion; there is no constipation or urinary trouble, but there is a constant leucorrhœa and the discharge is often streaked with blood.

Operation.—Incision in the median line of the abdomen 8 cm. long; over two gallons of ascitic fluid escaped; the left tube was very much enlarged and thickened; the ovary was not involved. The tube was excised close to the cornu of the uterus. The right adnexa appeared normal; wound closed with catgut and silk in layers. The protruding cul-de-sac of Douglas was then opened from below, emptied of its contents—a large amount of ascitic fluid—and the vaginal fornix, which was so redundant as to protrude at the vulva, was removed and its edges closed with catgut sutures. The uterus was everted and packed with iodoform gauze. There was nothing removed from the uterus which led to any suspicion of its containing a neoplasm. The patient, though fractious and unmanageable, made an uninterrupted recovery, leaving the hospital at the end of the third week.

MACROSCOPICAL APPEARANCE.

The mass consists simply of the left Fallopian tube. Its uterine end tapers abruptly and the abdominal end is the seat of an exuberant, cauliflower-like growth of new tissue which appears to have burst forth from the tube (Fig. 1).

⁵⁷ Meditsina, iii, p. 181, 1891, St. Petersburg.

⁵⁸ Wien. klin. Wchnsch., 1894, vii, p. 572.

⁵⁹ L. c., p. 455.

⁶⁰ L. c., p. 272.

⁶¹ L. c., p. 360.

⁶² L. c., p. 116.

⁶³ This case was briefly reported at the Chicago Gynecological Society, December 15, 1899, by Dr. Newman and myself.

The tube forms a small U-shaped bend, the convexity of which is upward. The middle of this convolution measures 1.5 cm. in diameter. It then bends downward and becomes greatly dilated. Its external surface is covered with a smooth, glistening, unbroken serous membrane which contains many circularly arranged blood-vessels. All signs of fimbriæ at the outer end have disappeared. At the external end is an abrupt termination of the smooth serous covering which is overrun with tissue grown out of the abdominal ostium. This new tissue consists in part of small, smooth nodules which vary from .6 and .8 to 1.5 and 2 cm. in diameter and of shaggy, rough tissue between the rounded parts. This outgrowth is spread over more of the under surface of the tube than elsewhere; it is very friable. The ovary and its ligament form a pedunculated appendage to the tumor mass and is small as compared to the large tube (Fig. 2). The length of the growth is 13.5 cm. The ovary contains a large corpus luteum; the external surface is smooth. Just in front of the tubo-ovarian ligament is a small accessory tube measuring 28 mm., springing directly from the serous covering of the main tube; its stalk is 1 mm. in diameter; its outer end is dilated (Fig. 1). The weight of the entire mass is 250 grammes. The tumor was hardened entire, and without cutting, in Mueller's fluid and formalin (4 per cent), except a small, irregular mass detached from the external end; this was hardened in strong alcohol (95 per cent). When the hardening was completed the tube was sectioned through its long axis. The center was found occupied by a soft material of a gray color; it filled the canal, and extends between the projecting masses of tissue which fringe the lining (Fig. 3). The muscular coats are thin, but the mucosa by its proliferation has invaded the necrotic content of the tube for a distance which averages 1 cm. in all parts of the tube. The proliferating lining is dotted over with grayish, necrotic débris. The greatest accumulation of this material has occurred in the middle of the tube where it measures 2 cm. in diameter; at this point the remaining 5 cm. of the diameter of the tube is occupied mainly by the proliferating mucous membrane. The muscular and fibro-serous coats measure from 1 to 3 mm. in thickness. At the uterine end of the tube there is a large amount of necrotic material in the lumen and but slight proliferation of the lining; at the abdominal end this condition is reversed.

MICROSCOPIC APPEARANCE.

Sections were cut from points along the whole length of the tube and stained by various methods. The structure is essentially the same in all portions. Set upon the muscular coats, which are thin, are many papillary or villous growths. They are usually tenuous stalks of connective tissue covered with epithelium (Fig. 1), which branches and rebranches to form a tassellated lining (Fig. 4). The epithelium consists of many strata, of which only the deeper layers have a columnar type. The nuclei are oval and irregular and do not stain very strongly. The absence of a nuclear membrane and the arrangement of the chromatin in certain

nuclei betokens poorly preserved karyokinetic figures. This assumption is made certain by finding, after some search, certain masses of chromatin which are plate-shaped and, in other cells, the double plates of metakinesis. Such nuclei in process of division are quite numerous; they are as abundant in the outer strata as in the inner. In sections stained after the iron-hæmatoxylin method, these nuclei in various stages of division form black masses. In some of the dividing nuclei, in spite of the unfavorable fixation, the centrosomes and the pointed ends of the groups of achromatic threads may be seen. There are no more irregularities in these dividing nuclei than might be accounted for by the hardening process. The layers of cells often number ten to twenty and in the outer parts of the tumor near the abdominal end they are even more numerous. The many-layered appearance of the epithelium is not due to the thickness or obliquity of the section, for in very thin sections cut in paraffin and not more than one cell in thickness, at least four to six layers are present, and this is true for regions where the outer layers have undergone considerable necrosis, where, in fact, the tips of papillæ are buried in necrotic débris. In no place are any single rows of epithelium upon a basement membrane found, such as occurs in the normal folds of the tubal mucosa. With low powers of the microscope the epithelial character of these cells is not clearly evident because of the large size of the nuclei as compared with the scanty amount of protoplasm surrounding them. Even with the immersion objective some appear to possess very little protoplasm. The nuclei alone average about seven mikrons in diameter when they are circular; the nuclei of the columnar cells measure in their long diameter ten to eleven mikrons. Exceptionally very large nuclei may be found which measure 15 to 20 mikrons in diameter. In practically every nucleus of the resting cells there may be found small oval bodies colored a pale green, with the hæmatoxylin and eosin staining; with the iron and hæmatoxylin and considerable differentiation, these bodies are much darker. Very rarely two occur in the same nucleus; they are undoubtedly nucleoli; the peculiarity consists in their large size. Very often they equal in diameter one-third or one-fourth of the diameter of the nucleus; exceptionally they occupy one-third of the entire nucleus. The columnar shape of the cells close to the stroma is manifested more by the shape of the nucleus than by the cell body; in this region the nuclei are more closely arranged in palisade form.

On the edges of these villous growths where the epithelium is in contact with the necrotic material, and in places where the edges of papillæ are in contact, the epithelial cells have undergone degenerative changes. Here occur occasional nuclei, usually smaller, in which the chromatin is collected in a few granules which stain intensely with nuclear dyes, and such granules commonly festoon the inner margin of the nuclear membrane or form a few crescent-shaped masses on its lining. Such nuclei may appear devoid of cell bodies. More frequently the necrosis has resulted in shrunken and



FIG. 1.—Tubal carcinoma — anterior surface—natural size.
a.—Accessory tube.



FIG. 2.—Tubal carcinoma—posterior surface—natural size.
a.—Ovary.



FIG. 3.—Tubal carcinoma sectioned longitudinally (three-fourths of natural size).
a.—Uterine end.
b.—Muscular wall.
c.—Necrotic tissue.
d.—Papillary growth of the lining toward the lumen of the tube.

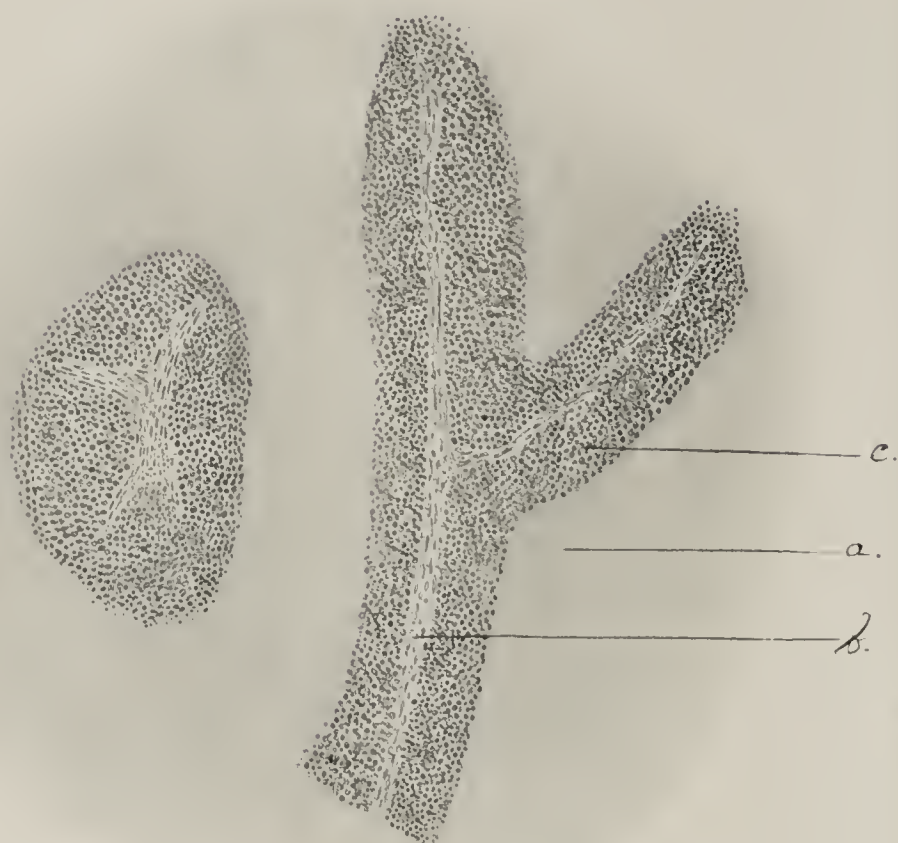


FIG. 4.—Villi that have been sectioned longitudinally and transversely; from the more central part of the growth.
a.—Necrotic tissue.
b.—Connective-tissue stalk.
c.—Epithelial cells in many strata.

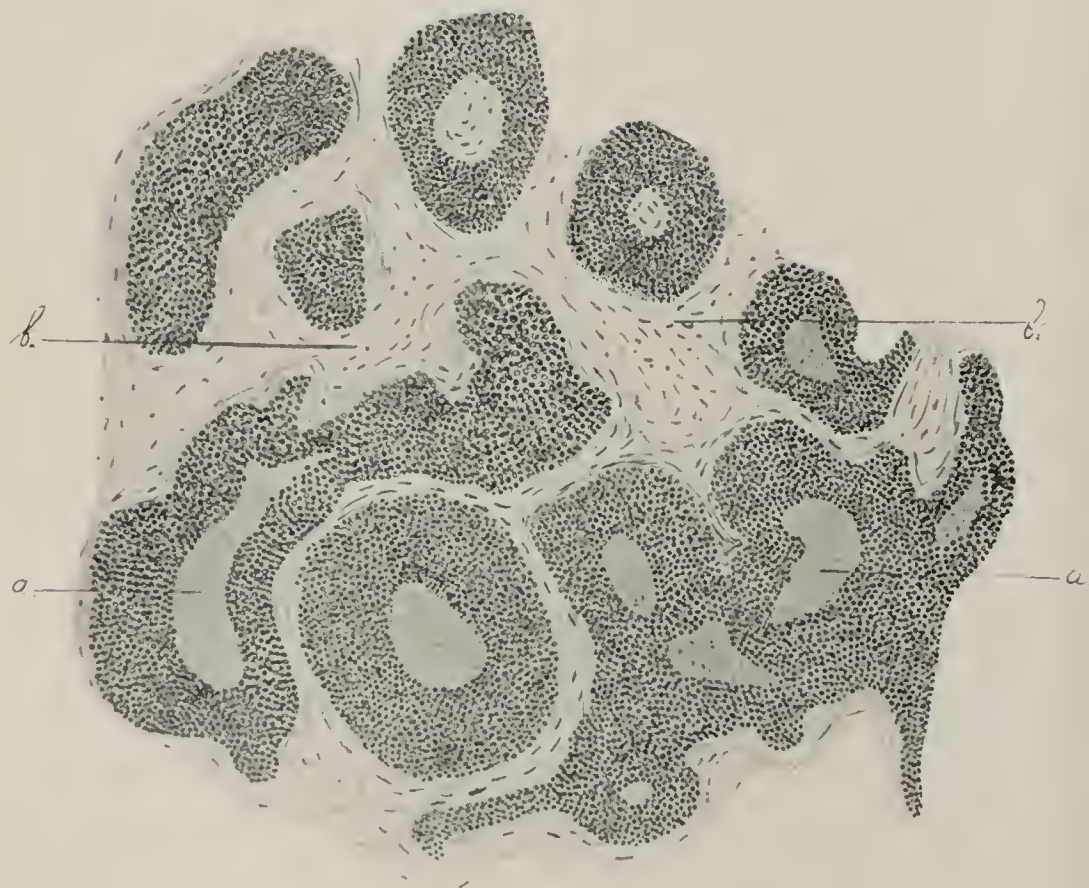


FIG. 5.—Intricate arrangement of stroma and epithelium in which it is difficult to interpret the appearances without the study of serial sections.
a.—Necrotic tissue.
b.—Stroma.

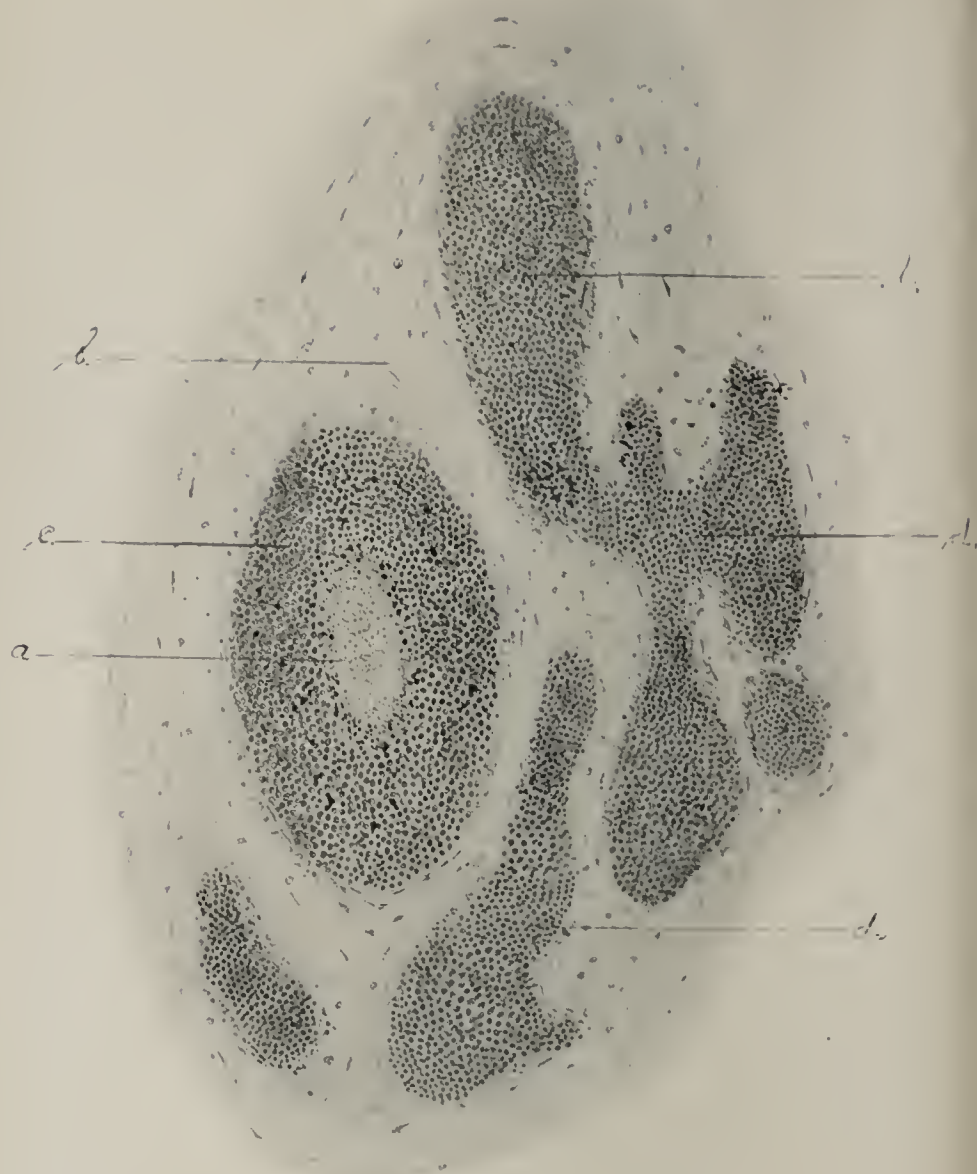


FIG. 6.—“Inverting type” of proliferation. The epithelium between the papillary growths has proliferated outward toward the muscular wall.
a.—Necrotic tissue.
b.—Stroma.
c.—Epithelium.
d.—Masses of epithelium lining cavities that have not been opened in this section.



FIG. 7.—Showing the outward growth of intervillous epithelium and the flattening of the thereby produced diverticula against the muscular wall of the tube.
a.—Diverticulum filled with necrotic tissue.
b.—Beginning papillary proliferation of epithelium into the diverticulum (cyst).
c.—Muscular wall of tube—only a part of which is shown.

irregular nuclei which stain deeply throughout. Some nuclei also have long, twisted and irregularly tortuous extensions. Upon the ultimate border occurs a zone composed of dust-like granules of chromatin. In the necrotic tissue in which the free ends of the papillæ are embedded, there may be found occasionally cells distinguishable by their shape and size which have, however, lost all power to react to nuclear dyes; they assume the same tint with eosin as the granular material in which they lie. Leucocytes are present in the epithelial covering of the papillæ, but only as isolated cells; they are never accumulated in foci. Although often of the polymorphonuclear type, there are also many with small round nuclei. In the layers of epithelium they are easily distinguished from the epithelial cells in process of division, but in the outer bordering zones of necrosis they lose their identity. The leucocytes are often present in the walls of the vessels of the stroma.

The stroma or connective-tissue stalks upon which the epithelium is arranged to form papillary growths is very delicate (Fig. 4). It consists of but little more than a vessel wall. On each side of the lumen of the vessel are from three to six layers of parallel long cells which resemble the cells of involuntary muscle. Their nuclei are slender and from 20 to 30 mikrons in length and possess rounded or abrupt, blunt ends. The margins of these cells are obscure when in contact; but in advantageous places it is possible to see that the cells, like the nuclei, are spindle-shaped. Where papillæ have been cut across, the ends of the divided nuclei of these cells appear round and the nuclear membranes are much darker than when in longitudinal planes. Elastic fibers (Weigert's stain) are present neither in the walls of the blood-vessels of the connective-tissue stalks nor in the layers of cells which surround the vessels. The endothelial lining of the vessels is well preserved and shows no changes. There is some fibrin in some of the vessels and a small quantity in the necrotic tissue between the papillæ; in either case it never consists of more than a delicate network, extremely irregular. In sections from all parts of the tube examined it is possible to find villous outgrowths, the epithelium of which has become completely necrotic, but in which the stroma has not entirely lost its staining properties. Such papillæ, stained with Van Gieson's stain, show prolongations of the stroma extending for even long distances into the necrotic material before their nuclei, too, suffer chromatolysis. In some papillæ the epithelium is entirely necrotic upon both sides for only a short segment of its extent, the fuchsin-stained stroma bridging over the defect.

It is evident from the foregoing description that the papillary growths in this tumor consist mainly of an epithelial covering of many layers and that the proliferation of these has been so marked that they have filled the tube entirely, distended it to a marked degree and have undergone a considerable necrosis. The necrotic tissue has filled the enlarged channel. These growths have been referred to as stalks, as villous growths; when cut directly across, their outline is circular. Such circular bodies lying in the midst

of the necrotic tissue have a striking appearance, since in certain sections they are found at considerable distances from any other tissue. Their outer margin is bordered by the dark circle of pycnotic nuclei and chromatin granules; the larger part of the body consists of the mass of epithelium with the radially disposed nuclei, and a small vessel containing numerous red blood-cells forms the center.

As might be expected, these villous growths have no regularity in their arrangement. The study of many sections cut in series shows that the entanglement is very intricate (Fig. 5). Arising from the wall of the tube, their course may be directly toward the lumen or oblique or even parallel to the wall. To complicate the arrangement, the villous growths frequently join one another as well as branch; consequently, in certain sections there may be seen at short distances from the muscular walls regions made up entirely of masses of epithelium, each mass consisting of a papilla cut obliquely or transversely, and containing in its center the blood-vessel. The edges of these clusters of epithelium may be in contact and the line of division difficult to find; in other places a narrow row of necrotic cells separates the epithelium of different papillæ; in yet other places the necrotic material has accumulated between them so that they appear well separated.

In deeper zones nearer the muscular walls still another peculiar appearance is obtained. Here the condition is reversed; the stroma borders the epithelium on the outside, and the epithelium lines a cavity filled with necrotic tissue (Fig. 6). The examination of serial sections shows that such cyst-like collections of cells are due to the growth outward, toward the muscular layers, of that part of the mucosa which intervenes between the villous prolongations; these outward growths, when cut across, appear like small cysts filled with necrotic tissue. As a rule the lining of these cavities at the inner margin is sharp and distinct. The layers of the epithelium are the same in character and number as those which cover the papillæ. It is essentially the same epithelium; the proliferation toward the lumen has resulted in villous growths; toward the muscular wall, in cavities; and these, when sectioned, appear like cysts. The necrotic material which fills them usually stains lightly and with eosin, but some are met with which are quite filled with chromatin granules; such cysts (so-called for convenience) have a darkly stained content. Naturally, such cavities are not always sectioned directly across; they often appear long and parallel to the muscular wall, or they are short and more oval. The muscular wall is bordered in this manner with but little interruption. It is obvious that the inter-papillary proliferation outward toward the muscular wall has met with an obstruction; the distention of the tube has not been able to keep pace with the proliferation of the epithelium. Sections occasionally show the following condition: the inner border of the muscular wall of the tube is covered with the same epithelium in strata as has been described upon the papillæ. This epithelium lines a cavity the opposite wall of which is quite distant (the width of

the field, Obj. 3, Ocular 3, Leitz) and from the opposite wall small villous growths project toward the muscular wall; the remainder of the cavity is filled with necrotic tissue (Fig. 7). These cystic formations in some sections, with the tissue in which they lie, form a zone of considerable width just inside the muscular coats.

The tissue between the cysts is made up of the same elements as those described in the stroma of the villus, except that between the cysts it is abundant, whereas in the villi it is insignificant. It contains the long spindle cells, in all respects identical with those found in the villi; also many vessels in which are little more than loose-walled sinuses. Scattered leucocytes are seen frequently both with round and with irregular nuclei. The greater part of the stroma is apparently formed by fibers; some of them stain red with Van Gieson's stain; most do not. There are no elastic fibers among them. Numerous slender capillaries, which are so delicate that a single red corpuscle fills the lumen completely, are conspicuous in some sections in the stroma; with the iron-haematoxylin stain, by which the red blood-cells are made almost black, such capillaries, filled with blackened cells, form a distinct delicate network.

Very peculiar appearances are caused by the occurrence in the stroma, in certain places, of collections of blood-serum⁶⁴—œdematous regions. The coagulated serum usually has small holes in it, oval in shape, which resemble the holes in the cells of a fatty liver; often leucocytes are found in the holes. The margins of the serum are beset with semi-circular spaces; both the oval holes and the marginal defects are due to the shrinkage of the coagulated serum. In such œdematous situations, and in the tissue of the bordering zones, are found large swollen cells in all stages of drop-sical degeneration; the wall of the cell forms a bag for the network produced by the vacuoles. Such vacuoles do not have the clear outline of holes which at one time contained fat. Often considerable fibrin occurs in the œdematous spots, and in places œdema is combined with hæmorrhage. Plasma or mast cells are not present in the œdematous districts or in the stroma elsewhere.

The question naturally presents itself: Are there any loose, unconnected, wandering epithelial cells in the stroma? A careful search for these was made in different ways. Many cysts were examined to see if at their outer margins there could be found any evidences of the proliferation of the epithelium outward into the stroma. Also many serial sections were examined to see if any of the collections of epithelium which form cysts were entirely unconnected and cut off; a third evidence of such a process was sought for, viz., cells in the stroma with nuclei in mitosis. All of these signs of invasion of the stroma by loose and wandering epithelial cells were absent. The proliferation of the epithelium has been *en masse*; by the proliferation of the tubal lining as a membrane; also by the production of a lining of many strata.

The muscular wall of the tube averages 1 to 2 mm. in width. The muscle fibers are few in number; sections stained by the picrofuchsin mixture reveal a large amount of fibrous connective tissue which takes a brilliant red color; this preponderance of fibrous tissue is especially marked in the inner half of the wall. The circular coat has undergone the greatest atrophy; only occasional strands of it are present.

The outer half of the fibro-muscular wall is more loosely arranged. There are many large, flattened blood-vessels in this portion and around them small aggregations of fat. In the inner one-half of the wall occur occasional clusters of lymphoid cells that show the effects of pressure, being greatly elongated and parallel with the fibers. Such lymphoid nodes made up entirely of cells that correspond to small lymphocytes occur in all sections. In a few sections there are islands of cells that present a different appearance; closely aggregated cells with pale nuclei form an elliptical clump that possesses a very definite margin. Careful examination fails to reveal any nuclear figures in these cells; their nuclei possess very little chromatin; their arrangement is quite irregular; for these reasons and the fact that no lining cells can be found for the spaces in which they lie, a conclusion was reached that these islands have resulted from the proliferation of the endothelial lining of lymph channels. Still other islands of cells leave no doubt but that the proliferating epithelium has penetrated deeply within the fibro-muscular wall. In a few sections, lying nearer the inner border of this wall, are irregular tubules lined with epithelial cells. The nuclei of the cells are long, occupy most of the cell and stain deeply. The cells are columnar and in places two or three strata in depth. Some of these tubules occur within lymph channels, for outside the deeper and more columnar cells the endothelial lining of the channel is easily recognizable. Since these deeper prolongations of the epithelium were found so seldom, no effort was made to prove their connection by serial sections with the more centrally located parts of the tumor. The ovary contained no tumor tissue.

From Dr. W. W. Sheppard, the family physician, it was learned that for some time after the operation the patient was "nervous and hysterical," but improvement was steady and she was soon able to be up and around the house a part of each day. About nine or ten weeks after the operation ascites reappeared and upon vaginal examination a tumor, the size of an orange, was found on the left side. The ascites was relieved by tapping two or three times, the first being done on November 1st. During the month of December Dr. Byron Robinson was called in consultation. He has informed me that he found the abdomen enormously distended by a large tumor and considerable ascitic fluid. The patient was sitting up and able to walk about the house; her general appearance was cachectic, pulse 120, temperature 100° F. The tumor arose from the small pelvis and upon vaginal examination was found to be fixed, except its uppermost portion, which was slightly movable. It was

⁶⁴ The fluid of the blood is readily coagulated by hardening in solutions which contain chromic acid or its salts.

located chiefly on the left side. The uterus was slightly enlarged.

Operation (by Dr. Robinson).—Upon opening the abdominal cavity with a long median incision the entire peritoneum was found studded with papillomatous growths which varied in size from those barely visible to some as large as a hen's egg. The larger ones were located in the lower, left quadrant of the cavity, and in this position were adherent to one another so as to form an irregular mass. There were approximately two gallons of a clear ascitic fluid, similar in tint to pale ale, in the cavity. The irregular tumor on the left side was firmly adherent to the left lateral wall of the small pelvis; it extended upward so as to be in front of the sigmoid; the omentum was firmly adherent to it, and in the omentum near the tumor and also in the adjacent mesentery were many small shot-sized and pea-sized warty growths. Most of these growths had a pale yellowish color and were like a fresh brain in consistency; some of the smaller growths appeared very vascular. All of the larger growths were removed.

Recovery followed the second operation without any special events. At present she is able to perform some of her customary household duties. The ascites returned gradually so that about five months after the second operation paracentesis was necessary for the patient's comfort; and it has been practiced every two or three weeks since. At one time eleven quarts were removed, at another twelve quarts; the fluid maintains its former characteristics. A sample of this fluid showed on examination the following features: sp. gr. 1007, alkaline reaction, a large amount of albumin, absence of sugar, a moderate amount of proteids (biuret reaction), absence of bile, and .3 of 1 per cent of urea. I received the tumor masses removed by Dr. Robinson after they had been in a weak aqueous solution (4 per cent) of formalin for several days.

Macroscopic.—They consist of three large masses and about a dozen smaller; altogether they weigh 1,350 grammes. The largest piece measures $16 \times 13.5 \times 4$ cm. and is disk-shaped; on section it presents a granular surface which resembles somewhat adipose tissue. Its external surface is smooth except for tag-like, torn adhesions. Its concave side has a furrowed and trabeculated appearance. The next smaller in size is very irregular in form, measuring $12 \times 10 \times 5$ cm.; it is very rough and nodular externally and in spots has been torn. The smallest of the large pieces measures $11 \times 7.5 \times 4.5$ cm., and on section is found to possess a much softened, necrotic center. One of its flat surfaces is quite smooth. All of the smaller masses are very irregular; some appear to be little more than fibrous tissue, others resemble the larger masses.

Microscopic (continued).—Sections were made of all the large growths, and some of the smaller, and stained by various methods. A large part of all the growths consists of necrotic tissue; many sections contain little else. The necrosis is most marked in and around the central portions; such necrotic tissue stains lightly or darkly according to the

degree of chromatolysis; varying degrees of œdema and quantities of fibrin occur as well as small hæmorrhages. In sections where necrosis is less marked, the appearance of the innermost parts of the tubal tumor are duplicated; here occur cross-sections of papillæ lying in the necrotic tissue which are in all respects similar to those in the tube in size, shape, paucity of stroma and number of epithelial strata; the epithelial cells contain similar large nucleoli. Karyokinetic figures, however, are much more numerous; often three, four or six dividing nuclei are present in a single field of the immersion objective (celloidin sections, 15 to 20 mikrons thick). The stroma of the papillæ—connective-tissue stalks—has its origin in a capsule which surrounds each metastatic growth more or less completely. The capsule is formed by long cells arranged parallel to the circumference whose oblong nuclei contain nucleoli which are barely visible; these cells are not arranged in layers, for the nuclei have been cut in all possible diameters; the cells resemble the "fibroblasts" of organizing granulation tissue. In sections of the various metastatic growths, and even in different sections of the same growth, the capsule shows large blood-vessels, regions of necrosis and of hæmorrhage and thrombosed vessels. In regions just internal to the capsule, where the papillomatous growths have been so luxuriant that the papillæ are in contact and a tissue has been produced which appears solid and granular, if the stroma be examined in such places *the connective-tissue cells are also found with mitotic figures*. They are never as abundant as the dividing nuclei of the epithelium; that the stroma or supporting tissue contains cells which are multiplying is beyond doubt; that these cells are the same as those which constitute the stroma is also certain, since all stages of multiplication by indirect division may be found and also for the reason that there are no other cells in the stroma with resting nuclei than those described. It may be inferred that this difference between the stroma of the papillæ in the primary tumor and that in the papillæ of the metastatic growths is due to more favorable conditions of nutrition; it is also possible that the more rapid proliferation of the epithelium, as is shown by the abundance of dividing nuclei, has in itself led to a proliferation of the cells of the framework, and that this has been sufficient in amount to allow the observation of occasional dividing nuclei in the stroma cells.

This condition of embryonal stroma and embryonal epithelium, since both contain dividing nuclei, has resulted in a line of demarcation where epithelium and connective tissue meet, which is much less distinct than similar lines of contact in the primary tumor. In regions close to the capsule, where there has been a rich growth of papillæ and necrosis has not occurred, the indistinct line of contact and the entanglement of papillæ renders it difficult to distinguish between epithelium and connective tissue. Some aid may be had from the columnar position of the nuclei of the epithelium on the stroma, but this does not always obtain; in other places the epithelium has contracted away from

the stroma so that a narrow space is present. The blood-vessels in the stroma have very little wall; they resemble the vessels commonly encountered in a small spindle-celled sarcoma.

Among the tumors of the Fallopian tube that can be considered as carcinomata, this case is unique in the following particulars: The os abdominale was evidently open, since there was not formed the usual sac, and invasion of the peritoneal surface and adjacent tissues probably took place via this opening by continuity of surface. The case is also remarkable in that large secondary tumor masses were removed from the abdominal cavity, the patient still living, although slowly succumbing to the disease.⁶⁵ The similarity

⁶⁵ The patient died February 18, 1901; through the kindness of Dr. Sheppard, a necropsy was secured, the details of which will be shortly published.

in method of growth and general histologic structure to proliferating cystadenomata of the ovary is continued in the comparative benignancy of the peritoneal metastases.

The appended table comprises 21 cases of carcinoma that were selected from 52 cases that have been reported as papilloma or carcinoma. 15 of the 52 were excluded by reason of insufficient data; of the remaining 37 some have been shown to be instances of hyperplasia of the tubal mucosa due to inflammation, a process usually combined with sacto-salpinx, that leads to the formation of benign localized growths whose position in the domain of tumors is very questionable, or to more diffuse growths that may possess some of the characteristics of malignancy; the latter resemble the carcinomata that develop in scars, burns or fistulae from long-continued irritation.

AUTHOR, TITLE AND PLACE OF PUBLICATION.	BILATERAL OR UNILATERAL.	CONDITION OF THE OPPOSITE TUBE.	CLOSURE OF OS ABDOMINALE AND FORMATION OF A SAC.	RECURRENCE OR RECOVERY. DEATH SOON AFTER OPERATION.	CONCERNING METASTASIS, INVASION OF ABSCESS CAVITIES, ETC.	CONDITION OF THE OVARIES.	REMARKS.
E. Senger: Ueber ein primäres Sarkom der Tuben. Centralbl. f. Gynäk., 1886, X, p. 601, Leipzig.	Bilateral.		In both tubes there occurred two dilatations or sacs.	Tumor found at necropsy.	In Douglas's pouch a small growth.	Both normal.	Reported as sarcoma.
E. G. Orthmann: Ueber Carcinoma Tubae. Ztsch. f. Geburtsh. u. Gynäk., 1888, XV, p. 212, Stuttg.	Right tube.	Pyosalpinx.	The outer end, greatly dilated opened into an abscess cavity.	Death on sixth day after operation.	The tumor had invaded two abscess cavities. A small nodule in the "excavatio vesico-uterina." A swollen lymph gland in the small pelvis.	Abscesses in both ovaries.	
A. Doran: Primary Cancer of the Fallopian Tube. Tr. Path. Soc. (London), 1888, XXXIX, p. 208.	Right tube.	Left tube at operation appeared small.	Outer end closed: a sac formed.	Recurrence; lived nearly eleven months after operation.	Lumbar glands invaded.	R.—cancerous.	At necropsy, tumor found in the uterine vesical and vaginal mucosa.
C. J. Eberth and R. Kaltenbach: Zur Pathologie der Tuben. Ztsch. f. Geburtsh. u. Gynäk., 1889, XVI, p. 357, Stuttg.	Bilateral.		L.—dilated to size of thumb. R.—larger (faustgrösse.)	Recurred in 18 months.	Subperitoneal nodules noted on the right tube.		Demonstrated first as carcinoma. Reported later as papilloma.
T. Landan and J. Rheinstein: Beiträge zur pathologischen Anatomie der Tube. Archiv f. Gynäk., 1890-91, XXXIX, p. 273, Berl.	Right tube.	Outer end closed and a sac formed that contained 500 ccm. of bloody, thin fluid.	Sac formed on right side.	Recurred in 10 months.	Ascites after the operation, with hard masses in the abdomen.	Normal.	
S. D. Michnoff: A Case of Primary Carcinoma of the Fallopian Tubes (Russian). Meditsina, 1891, III, p. 181, St. Petersburg.	Left tube.	Sacto-salpinx papillomatosa.	Left tube formed a sac as large as a large fist.	Recurrence in 7 months.	A cyst occurred at junction of right tube and ovary, size of a hen's egg; it was filled with clear fluid.	L.—ovary left in body, it was imbedded in adhesions. R.—normal.	
P. Zweifel: Vorlesungen über klinische Gynäk., 1892, p. 139, Berlin.	Bilateral.		Large sacs on both sides. L. tube 20 cm. long and 8 cm. thick.	Presumably recurrence, since patient died 1½ years after operation.		Normal.	
F. J. E. Westermarck and U. Quesnel: Ett fall af dubbelsidig kancer i tubae Fallopii. Nord. Med. Ark., 1892, XXIV, Nr. 2, p. 1, Stockholm.	Bilateral.		Sacs formed on both sides—larger on left.	Recurrence: death in five months.	Invasion of cyst of right ovary. No exudate in peritoneal cavity at necropsy. Lymph glands of small pelvis invaded. T.—nodules found in the liver at the necropsy.	L.—ovary cystic. Monocular cyst size of an orange.	Carcinoma of the cervix found at the necropsy.

AUTHOR, TITLE AND PLACE OF PUBLICATION.	BILATERAL OR UNILATERAL.	CONDITION OF THE OPPOSITE TUBE.	CLOSURE OF OS ABDOMINALE AND FORMATION OF A SAC.	RECURRENCE OR RECOVERY. DEATH SOON AFTER OPERATION.	CONCERNING METASTASIS, INVASION OF ABSCESS CAVITIES, ETC.	CONDITION OF THE OVARIES.	REMARKS.
R. Kretz: Zur Casu- istie der Papillome der Eileiter. Wien. klin. Wchnsch., 1894, VII, p. 572.	Bilateral.		L.—tube 17 cm. long and 6 to 8 cm. in diameter. R.—tube similar. Both closed ex- ternally.		Small subperito- neal nodules noted, exter- nally on both tubes. Invasion of the lymph channels, (histologic examination).	Unknown.	Reported as papillomata. Kretz considers the case similar to that of Eberth and Kaltenbach.
W. Fischel: Ueber einen Fall von pri- mārem papillärem Krebs der Mutter- trompeten. Lapa- rotomie, Heilung, Ztsch. f. Heilk., 1895, XVI, p. 143.	Bilateral (?)	Condition of left tube not posi- tively known. It was imbedded in adhesions and not removed.	R.—tube formed a sac 8 by 4.5 cm.	Recurrence: death seven months after the operation.	Small nodules on external surface of right tube. Abdominal cavity contained clear ascitic fluid.	Unknown.	Part of the cyst of the right tube possessed a smooth wall covered by a single layer of short epithe- lium.
A. Rosthorn: Pri- māres medullares Carcinoma tubæ. Ztsch. f. Heilk., 1896, XVII, p. 177.	Right tube.	At necropsy left tube found to contain meta- static (?) tumor nodules.	Sac formed by right tube sup- posed to be pyosalpinx.	Recurrence: death six months after first operation.	Inguinal glands removed at a second oper- ation. Retro- peritoneal glands found invaded at the necropsy.	Cyst of right ovary.	Necropsy by Chiari.
T. J. Watkins (and E. Ries): Exhibition of unique microscopic sections of papilloma and carcinoma of the tubes, etc. Am. Gyn. and Obst. J., 1897, XI, p. 272, N. Y.	Bilateral.		Both tubes large and formed by four convolu- tions; both closed extern- ally.	Recurrence: death seven months later.	Ext. end of the right tube con- nected to a mass 4 × 4 × 5 cm. This contains a cen- tral cavity beset with several wartlike growths. Metastatic carcinomata on the ovaries and on post. surface of right tube. Collec- tions of tumor cells found in lymph channels of wall of left tube.	L.—ovary many corpora candi- dantia.	Condition of right ovary not clear.
E. Falk: Fortschritte u. gegenwärtiger Stand der vaginalen Operations technik. Therap. Monatsh., 1897, XI, p. 313, Berl.	Left tube.	Unknown.	Left tube closed externally. Sac formed.	Recurrence: death seven months after operation.		L.—ovary normal.	Tumor found in the uterus in mucosa near right ostium and diagnosed as sarcoma was supposed to be responsible for recurrence and death.
K. Eckardt: Ein Fall von primārem Tub- encarcinom. Arch. f. Gynäk., 1897, LIII, p. 183.	Left tube.	Normal. (Doran).	Sac formed by the left tube size of child's head.	Healthy a few months later. Subsequent history un- known.	Subperitoneal elevations, size of hazel-nut, make external surface irregu- lar.	Both normal.	Broad ligament shortened by invasion of the tumor.
A. H. Pilliet: Épithé- lioma de la trompe utérine. Bull. Soc. Anat. de Par., 1897, XI, p. 956.	Right tube.	Unknown.	Cavity in the right tube oppo- site ovary.	History not known.	Invasion of the lymph channels, (histologic ex- amination.)	Condition of left ovary unknown. R.—invaded by tumor in its outer part only.	
C. H. Roberts: A Case of Primary Carci- noma of the Fallop- ian tube. Tr. Obst. Soc. London, 1898, XI, p. 189.	Right tube.	"The left tube inflamed and closed."	Outer end of right tube closed: sac formed.	Well ten months later.		Normal.	Very brief histo- logic descrip- tion.
J. Fabricius: Beiträge zur Casuistik der Tubencarcinome. Wien. klin. Wchnsch. 1899, XII, p. 1230.	Left tube.	At first operation the right adnexa appeared nor- mal; at second, thickened.	Supposed to be a pyosalpinx until it was cut.	Recurrence five months later when a large mass filled the right half of the pelvis.		Unknown.	At the first oper- ation masses removed were pronounced papilloma. At the second operation when radical removal was found to be impossible, masses were removed that were pro- nounced carcinoma.

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J. Fabricius: Idem.	Right tube.	L.—adnexa appeared normal at the operation.	Abdominal opening leads into a cyst.	Recurrence: five months after first operation left adnexa and uterus were removed.	Carcinomatous invasion of the cyst on right side. At the second operation it was found that the entire peritoneum was beset with small tumor nodules. The metastatic nodules on the outer surface of the uterus were examined and pronounced adenocarcinoma.	Right ovary enlarged but otherwise normal.	After second operation a large cyst developed that reached upward to the navel and finally evacuated through the rectum.
Danel: Essai sur les Tumeurs malignes primitives de la Trompe Utérine, 1899, Paris.	Left tube.	Appeared healthy at operation. Not removed.	Left tube formed a sac.	Recurrence took place on the right side.	Many peritoneal growths on the uterine end of the tube. Enlarged glands in the adhesions around left tube. Tumor cells found in the lymph channels. (Histologic examination.)		
B. Friedenheim: Beitrag zur Lehre vom Tubencarcinom. Ueber ein primäres, rein alveoläres Carcinom der Tubenwand. Berl. klin. Wehnseh., 1899, XXXVI, p. 542.	Left tube.	Unknown.	No sac formed.	History subsequent to operation unknown.	Left tube and tumor adherent to colon. Left parametrium infiltrated with tumor masses.	L.—smooth externally, size of a walnut, contained small cysts.	Tumor said to have had its origin in an accessory tube.
E. Mercelis: Primary carcinoma of the Fallopian tube. N. Y. Med. J., 1900, LXXII, p. 45.	Right tube.	Left tube removed. Condition not described.	Right tube 4 cm. in greatest diameter. Outer end closed.	Recurrence on right side 18 months later.	Outer end of right ovary invaded by tumor.	L.—ovary small and firm—not removed. R., the seat of chronic interstitial changes.	

REPORT UPON A CASE OF GONORRHOEAL ENDOCARDITIS IN A PATIENT DYING IN THE PUERPERIUM; WITH REFERENCE TO TWO RECENT SUSPECTED CASES.

BY NORMAN MACLEOD HARRIS, M. B.,
Associate in Bacteriology, Johns Hopkins University.

AND

WILLIAM M. DABNEY, M. D.,
Late Resident Obstetrician, Johns Hopkins Hospital.

CASE 1.—I. T., aged 19, unmarried, was admitted to the Obstetrical Department of the Johns Hopkins Hospital on February 13, 1900, complaining of fever and weakness which she thought were of puerperal origin.

Family History.—Negative as far as could be ascertained.

Personal History.—There is no history of the ordinary diseases of childhood, nor of any acute infectious disease. She has never had rheumatism, and states that previous to the onset of the present illness she has always been a healthy woman.

Marital and Menstrual History.—The patient is unmarried, and has had no previous children or miscarriages. The menstrual history is normal in all respects.

Present Illness.—The patient states that she was confined

on January 19, 1900, after a hard but non-instrumental labor at term. (Child living.) During the course of the labor frequent vaginal examinations without aseptic or antiseptic precautions were made by those in attendance, and the third stage of labor was furthermore complicated by a retained placenta, which, after several attempts was removed manually, likewise without precautions. On the fourth day of the puerperium she was seized with a chill, followed by fever, and, later, sweating, and these symptoms have recurred regularly every day since then. Other symptoms have been headache and general pain in the limbs, nausea and vomiting, the latter at times marked, and almost complete loss of appetite. For the past few days she has had, in addition, a rather constant cough, accompanied by some pain in the

side. The patient says she has been confined to bed practically ever since labor, and, though she has felt at times better than at first, she has grown progressively weaker.

Physical Examination.—The patient's mental condition is very dull apparently, answering questions poorly, and only when repeated and asked in a loud voice. Well-formed and well-nourished woman, marked anæmia present, the lips and mucous membranes being almost bloodless. Temperature on admission 102.4° F., pulse 120.

Thorax.—Well formed. Respirations rather hurried, with an occasional short, sharp cough.

Lungs.—Expansion fair, equal on the two sides. Vocal fremitus normal. Percussion note normal throughout. On auscultation at the base of each lung, a few very fine crackles are heard on deep inspiration, and here and there over both lungs an occasional medium moist râle. The breath-sounds are normal.

Heart.—The point of maximum impulse is neither visible nor palpable. No thrill or shock on palpation. Apparently no increase in the area of cardiac dulness. On auscultation at the apex both sounds are practically obliterated by a to and fro murmur, the systolic being the louder and more intense. Both murmurs are transmitted and well heard in the axilla. Preceding the systolic murmur a rather loud rumble is heard at the apex, which is likewise transmitted to the axilla. Over the body of the heart both murmurs are well heard. Over the base the systolic murmur becomes diminished in intensity, the diastolic more clear-cut and marked. The presystolic rumble is lost. The pulse is markedly collapsing in character, and there is a distinct capillary pulse present.

Abdomen.—Looks normal. No rose-spots are visible. There is no distension and the abdomen is everywhere soft on palpation.

Spleen.—Not palpable.

Liver.—No apparent increase in dulness. The edge is just palpable at the costal margin.

On palpation no mass can be felt in the pelvis on either side or in either iliac fossa.

Legs.—Edematous and slightly swollen. No swelling or other changes in the joints noted.

Following admission on the morning of February 13th, the patient had several vomiting spells, attended by signs and symptoms of collapse, her skin becoming cold and clammy, and her pulse dropping from 120 to 80-90 to the minute, with an occasional intermission. When first seen in the afternoon, several hours after admission, the patient looked septic, but seemed to be in fair general condition. Temperature at this time was 101.6° F., pulse 112 to the minute, rather weak and of poor volume and tension. When seen again about 7.30 P. M., she was found to be in far better general condition, though markedly drowsy. Her history was taken at this time, and the physical examination made. A provisional diagnosis of ulcerative endocarditis of the aortic valve, secondary to puerperal infection, of probably strep-

toococci origin, was made at this time. During the night the temperature again rose, reaching its maximum, 103° F., about midnight, pulse 120 to the minute and much weaker. The general condition became very much worse, there being marked prostration with drenching sweats as a particularly noticeable feature. About 8.30 A. M., February 13th, the temperature had fallen to 100.8° F., the pulse, 80 to 90 to the minute, and of poor volume and tension. Attacks of vomiting, attended by increasing signs of collapse, continued, and the general condition seemed very much worse than at a corresponding time last night. Material for taking a culture from the uterus was secured about 9 A. M., a fair amount of bloody lochia being obtained.

The perineum was found practically intact. On vaginal examination the uterus was found enlarged, apparently normally involuted, according to the history, and slightly retroposed. The cervix was slightly torn. The adnexa seemed normal.

About an hour and a half later, the condition remaining about the same in the meanwhile, the patient had another very severe attack of vomiting, with great collapse and much sweating, so that, in spite of stimulation and subcutaneous infusion of normal salt solution, the pulse, which had fallen to 60 to the minute and was very weak and intermittent, gradually became weaker and finally ceased at the wrist, the patient dying shortly thereafter.

Blood.—An examination of a fresh blood specimen was made about 9.30 A. M., February 13th, and found negative for malarial organisms. Apparently a leucocytosis was present.

Urine.—Examination of a specimen obtained during the night showed a distinct whitish flocculent precipitate, a distinct trace of albumin, no sugar, and no diazo-reaction. Microscopically a number of hyaline and some epithelial and pus casts, a number of pus cells and some epithelial cells, and a number of micro-organisms, some of which showed motility, were found.

Uterine Culture.—Cover-glass specimens, stained with gentian-violet, showed a few epithelial and some pus-cells, and possibly an occasional coccus or in doubtful pairs, but so few in number that it was impossible to say whether they decolorized by Gram's method or not. Cultures taken on bouillon, agar plates (2 dilutions), and anaërobic glucose agar, all remained sterile.

The history pointing so clearly to puerperal infection, the possibility of the gonorrhœal nature of the trouble was not thought of, and, in consequence, no attempt was made to obtain the gonococcus culturally from the uterus.

PATHOLOGICAL REPORT.

Autopsy No. 1487, February 14th, 7.45 P. M., by Dr. W. G. MacCallum.

Anatomical Diagnosis.—Acute vegetative and ulcerative endocarditis, involving aortic, tricuspid and pulmonary artery valves. Acute splenic tumor. Infarction of spleen. Catarrhal cystitis. Puerperal uterus.

The body is that of a young, well-nourished woman, whose breasts are in the puerperal state.

Upon section, the peritoneal cavity is found to contain very little fluid, and the serous membrane is smooth and glistening.

The pelvic cavity contains a small amount of a brownish, slightly turbid fluid.

The *omentum* is bound down between the liver and spleen by fresh adhesions over a small area.

The *pericardium*, upon being opened, contains a small amount of feebly turbid fluid, but its serous surfaces are smooth and glossy.

The *Heart*.—Weight 325 grams. The epicardium is smooth. The right auricle is normal. The foramen ovale is open to the extent of 3 mm. The ductus Botalli persists as a cord.

The *tricuspid valve* is delicate. Upon the posterior leaf, abutting upon the septum ventriculorum, is a large lobulated vegetation which begins at the base of the valve and extends to its edge, hanging into the intervalvular space on the auricular surface of the valve. A granular mass also exists behind the valve, between it and the septum and lying upon the latter. The leaflet lying to the left of this as the heart is opened, shows a few minute pin-point translucent elevations on its auricular surface. The larger lobulated vegetations are opaque and yellowish and surmounted by soft post-mortem clots.

The *pulmonary artery valves* are delicate. At the junction of the right and left leaflets are small translucent vegetations on the ventricular surface.

The left auricle is normal.

The mitral valve is normal.

The *aortic valves* are most extensively involved, the posterior segment alone being free from vegetations. The left segment is surmounted on the ventricular side by a large mass of lobulated vegetations which extend down on to the ventricular wall. There is considerable roughening of the endocardium of the ventricle below the right segment also. The inner surfaces of these two segments in the sinuses of Valsalva are roughened and covered by soft dark-colored post-mortem clots. From the right sinus of Valsalva a probe can be passed through an opening in the septum ventriculorum into the vegetations on the ventricular side in the right ventricle behind the tricuspid valve. This opening has probably been caused by an extension of the inflammation through the septum.

The *heart muscle* is rather soft and brown in color.

Measurements: Circumference of tricuspid valve, 12 cm.; right ventricle, 8.5×4 cm.; circumference of mitral valve, 8 cm.; left ventricle, 7.5×12 cm.; circumference of aortic valve, 7.5 cm.

The *lungs* present a moderate degree of œdema; otherwise they appear normal.

Spleen. Weight 300 grams. Measures $18 \times 8 \times 6$ cm.

Excepting over two areas, one on the anterior surface

where the organ touches the liver, and the other at the posterior edge, the spleen is quite smooth. Corresponding to those areas of roughness the spleen is indurated and elevated. The anterior area is adherent to the liver by fresh adhesions, whilst over the posterior area are found a few fibrous adhesions only.

On section, these elevated firm areas are found to present the features of typical anæmic infarcts and are wedge-shaped. The spleen is soft and light purple in color. The great increase in bulk being in white spleen pulp. The Malpighian bodies are greatly enlarged and prominent, with irregular margins, measuring 3 mm. in diameter. The splenic pulp proper is not very greatly increased, but seems very soft and succulent.

The *Liver*.—Weight 1600 grams. Surfaces are quite smooth excepting where the organ is adherent to the spleen.

Gall-bladder and ducts are normal.

On section, it is soft and flabby and greasy to the touch. The lobules are quite definitely marked out; the centers being translucent, beyond them comes a congested zone, then outside of it is a zone of pallor and yellow opacity.

The *Kidneys*.—Each weighs 175 grams, and in all respects are alike apparently. They are slightly larger than normal, and the capsules strip off readily. The stellate veins are markedly injected, and between them the parenchyma has a grayish look.

On section, the cortex is thickened and measures from 5-8 mm. The striations are fairly well marked. The glomeruli are visible, but there is, however, some opacity and an appearance of being much swollen in the labyrinthine portion. The lines and dots of yellow opaque material are quite noticeable. The pelves contain a thick yellowish fluid, but they are not, however, especially injected.

The ureters are apparently normal.

The *urinary bladder* contains a small quantity of thick, yellowish puriform fluid, and the mucosa is in places deeply injected.

The *uterus* is enlarged and soft. The mucosa is somewhat congested, but there is no sign of inflammation (measurements of organ not given).

Fallopian tubes and ovaries are normal.

Lymphatic glands are nowhere especially enlarged.

The *bone-marrow* (femur) is somewhat reddened.

Other organs and tissues appear normal.

MICROSCOPICAL EXAMINATION OF TISSUES.

Heart muscle shows œdema and fragmentation (?).

Lungs also show general œdema, leucocytosis in blood of all vessels, and some local atelectasis.

Mammary glands show evidences of being in the normal state of lactation.

Spleen shows a state of general enlargement. The portion containing the infarction could not be found, having been inadvertently mislaid.

Liver presents evidences of chronic passive congestion with fatty metamorphosis.

Kidneys. A moderate degree of parenchymatous nephritis is noted, accompanied by a few foci of small round cells, which also occur in the walls of the larger arteries.

Intestines exhibit simply post-mortem degeneration, and evidences of leucocytosis in their blood-vessels.

Fallopian Tubes. Mucosa normal; blood-vessels give evidence of a leucocytosis.

Uterus. Sections were cut from three sites:—

(a) Cervix (including part of vaginal portion).

(b) Body (1, about the middle; 2, at the fundus).

These were stained in hæmatoxylin and eosin, methylene blue, by Weigert's and by Gram's methods.

(a) *Cervix*, on being stained in hæmatoxylin and eosin, presented the following features: The vaginal portion gave evidence of post-mortem degeneration only; likewise in the lower part of the canal similar changes are found, and dense masses of material staining blue in the hæmatoxylin can be made out readily in small clefts in the disintegrated tissue, being in all probability bacteria.

The mucosa of the upper portion of the canal shows no evidence of post-mortem change; it appears quite ragged and adhering to it in places are masses of what seem to be broken down red blood-corpuscles.

The submucosa is much richer in small round cells than is normal, and scattered about in moderate numbers are phagocytic cells containing altered blood pigment. In places where evidences of mucous glands exist, it is found that they are choked with shed epithelium, at times retaining its columnar form and at others being changed into granular detritus staining well in eosin and showing much nuclear debris.

Throughout the remainder of the section is noted a more or less well developed degree of œdema, best marked towards the parts beneath the mucosa. This œdematous fluid contains large numbers of small round cells, a few plasma cells, and moderate numbers of large mono- and polymorphonuclear cells which frequently are seen loaded with altered blood pigment, few in number and located deeply in the lower portion of the section, but higher up much more numerous and approach the mucosa, where they may be found lying in close contact to the deposits of broken down red blood-corpuscles.

The blood-vessels everywhere are greatly dilated and show evidence of marked leucocytosis, in which the polymorphonuclear cell prevails, but both large and small mononuclear cells are by no means scarce.

The arteries show no signs of either peri- or endarteritis, but in some instances their walls are thickened, due to hypertrophy of the muscular coat. Amongst the larger arteries can be seen at times small, irregular areas of a hyaline nature which stain brightly with eosin. The vasa vasorum give no evidence of inflammation.

The veins, especially along the course of the smaller ones, show at their peripheries considerable small, round-cell accompaniment.

Stained with methylene blue, the section presents no definite signs of the existence of micro-organisms. Notable, however, is the presence of numerous mast-zellen, more numerous in the deeper portions of the section than in the superficial parts.

Gram's stain, with Bismarck brown as counter-stain, simply brings out the presence of mast-zellen even more sharply than with methylene blue, but presents no signs of bacteria.

Weigert's stain shows no bacteria to be present.

(b) *Body of Uterus.*—Stained in hæmatoxylin and eosin.

Mucosa much thinner than normal. No columnar epithelium found. No placental tissue was noted. A few mucous glands could be identified and were found filled with shed columnar epithelium, mucus and some small round cells.

The general condition is similar to that described under cervix section, but, if anything, the small round cell infiltration is more intense, especially between the muscle-bundles.

The arteries show the same hyaline masses and there is no inflammation of the vasa vasorum. Occasionally seen in section from fundus, but more noticeably in the section from the middle portion of uterus, is a great thickening of the adventitious coat of the larger arteries and so dense that in places it resembles old dense hyalinized fibrous tissue. In these arteries the lumina can scarcely be traced and, in fact, a few show no lumina whatever, and their general course is a very tortuous one.

Sections stained in methylene blue, Gram's or Weigert's stains, show no evidence of bacteria, but as before in cervical sections, show presence of mast-zellen whose granules at first glance might be mistaken for cocci.

Coverslip preparations were made from

(a) the valvular vegetations,

(b) the pericardial fluid,

(c) the splenic infarct,

(d) the pelvis of left kidney,

(e) the contents of the urinary bladder.

Negative findings were recorded for (e), (c) and (d). Slips from the vegetations showed the presence of large numbers of cocci, occurring singly, in pairs, in fours and in clusters; also, in numerous proportion, the various kinds of leucocytes, the polymorphonuclear type greatly preponderating. The cocci for the most part appeared lying free, but not infrequently they occurred within cells. Typical biscuit-shaped organisms were by no means the rule. They readily decolorized by Gram's method of staining.

The preparations from the urinary bladder exhibited several varieties of bacilli and cocci, but of the latter none could be said to resemble the gonococcus.

Cultures.—Unavoidable necessity delayed the use of special media for fifteen hours, but cultures in plain agar were made at once from

(a and b) Aortic and tricuspid vegetations.

(c) Splenic infarct.

(d) Heart's blood.

(e) Left kidney.

(f) Urinary bladder.

These cultures were poured into Petri dishes and incubated at 36.5° C. for 48 hours and then examined.

Results on plain agar:

(a) Aortic vegetations yielded the gonococcus, *Streptococcus pyogenes*, *Bacillus coli communis*.

The isolation of the gonococcus on the plain agar was due to its having developed in a small fragment of blood-clot which had been carried over in making the culture. It was positively identified as such by its inability to grow on plain agar or ox-blood serum, but growing luxuriantly upon hydrocele fluid agar, and finally by decolorizing in Gram's stain.

(b) Tricuspid vegetation gave the above organisms with the exception of the gonococcus.

(c) Splenic infarct remained sterile.

(d) Heart's blood gave bacillus.

(e) Kidney was grossly contaminated by bac. subtilis.

(f) Urinary bladder yielded the *Streptococcus pyogenes*, *Bacillus coli communis*.

Cultures in hydrocele fluid agar were made from

(a) and (b) Vegetations on aortic and tricuspid valves.

(c) Splenic infarct.

These were incubated for 48 hours at 36.5° C. and then examined.

Three types of colonies were found, resembling those of *B. coli communis*, *Streptococcus pyogenes* and gonococcus. Transfers were made at once of the two former organisms to plain agar-slants, and of the latter to hydrocele fluid agar and plain agar-slants. Typical growths of the colon-like bacillus and of the streptococcus were obtained on the plain agar, and upon the hydrocele fluid agar isolated colonies identical with those of gonococcus grew out. Strange to relate, of fifteen plain agar-slants inoculated as checks from the suspected gonococcus colonies, two showed slight but definite growth of a scarcely perceptible nature, which, upon examination, yielded a diplococcus identical in morphology and tinctorial reaction with the gonococcus. These two growths were transferred again to plain agar and also to hydrocele fluid agar with the result that upon the latter medium only did development occur, and further attempts failed to produce growth from these hydrocele fluid cultures upon plain agar.

This same result Dr. Young states has at rare intervals come under his notice also in the work of the genito-urinary clinic.

That the third type of organism isolated from these plates was the gonococcus is proven by its failure to grow upon plain agar (excepting the two instances noted beforehand) and upon ox-blood serum and other ordinary media, by its being able to grow upon media containing human blood (as noted on the plain agar plate) or human serum when grown at 37° C., and by its inability to retain the stain when treated by Gram's method.

CASE 2.—Medical No. 9274. W. A., æt. 28.

Was admitted to Ward F on November 25, 1898, being

sent in as a supposed case of typhoid fever. Patient complained of pains in the stomach, heart and kidneys.

Family history was of no importance.

Past History.—As a child he had measles and possibly typhoid fever. At 22 years of age he had an indefinite illness which was treated as smallpox, typhoid fever and diphtheria, during the course of which there occurred a swelling below the right ear which, on being opened, discharged pus. There is an indefinite history of malaria following three weeks after the above illness, which was cured by quinine.

Patient never had any urinary disturbances nor pains in lumbar region. He had gonorrhœa three years ago, accompanied by an inguinal bubo which did not suppurate; there were no other sequelæ.

The patient denied syphilis; he was a moderate drinker.

Present illness began on September 26th. He partially recovered, but soon got worse again. He first noticed a general weakness, and had "dumb chills" for three weeks daily, followed by moderate sweats; there was neither nausea, nor vomiting, nor herpes, nor diarrhœa. He then got steadily worse and was confined to bed for 4-5 weeks. Improvement followed so that he got out of bed and staid in his room one week, then went about the house, but four days later he had a relapse, which, the patient thinks, turned into typhoid fever. This happened about a month ago; since then he was in bed until two weeks ago, when he got up and walked around, but owing to swelling of his legs and consequent stiffness, he returned to bed. In this period he had herpes and night-sweats, although during the last three weeks the latter have been absent; likewise he experienced for the first time palpitation of the heart and shortness of breath, accompanied by a rather bad cough, worse at night. The expectoration is of a whitish color. Paroxysms of coughing at times caused vomiting, chiefly at night and very early in the morning.

The œdema of the legs has lasted two weeks and is no worse than when it began upon the third day of this relapse.

Bowels are irregular, and there is some increased frequency of micturition, especially at night.

Upon the day of admission (November 25th) he had chilly sensations and his temperature rose to 101.8°, falling to 97° at 8 A. M. on the 26th.

The physical examination showed that patient was anæmic, and a puffy condition of eyelids was noticeable. The pulse was of good volume but irregular in force and rhythm, with a suggestion of a collapsing quality. Rate 26 to quarter minute. The heart was found to be enlarged, the point of maximum impulse being in the fifth interspace, 8.5 cm. from mid-sternal line. A thrill was felt.

Upon auscultation, at the base of heart a short systolic murmur was noted, traceable to the anterior axillary line. Over body of heart a faint diastolic murmur was heard, becoming louder upon passing upwards and inwards. A friction rub was heard at the left of sternum in the second and third interspaces, and in the same situation to the right of sternum. At the aortic area a systolic murmur was quite

readily heard. Over the pulmonic area the heart-sounds had a loud rumbling quality and the second sound was markedly accentuated and reduplicated. The lungs showed the presence of a few moist râles at the bases. The presence of fluid in the abdominal cavity was made out. Œdema was marked in the feet and legs. There was no general glandular enlargement.

Upon the 30th he seemed more comfortable, but the cardiac conditions became more pronounced and the lungs presented evidence of congestion. And upon the morning of December 1st he was cyanotic and drowsy and had an annoying cough. The heart and lungs presented nothing new. Œdema was most noticeable in the tissues of face. Less urine was voided. At 8 P. M. he said he felt comfortable, but at 9.15 the nurse found him dead.

His blood was examined on day of admission and showed hæmoglobin 18 per cent, leucocytes 8600, red blood-corpuscles 1,768,000. On the 28th of November the leucocytes rose to 14,000, but upon the following day had fallen to 8000, whilst hæmoglobin rose to 31 per cent.

Examination of the urine on the day of admission presented the following condition: S. G. 1.013; reaction acid; much albumin present; sugar absent; many epithelial casts, pus-cells and small, round, nucleated cells present; a few red blood-cells noticed. Diazo-reaction absent. Albumin was present until the day of patient's death and was estimated upon several occasions to vary from .8-1.2 per cent.

ABSTRACT FROM THE PATHOLOGICAL REPORT.

Anatomical Diagnosis.—Acute ulcerative endocarditis of pulmonary valve; ascites; hydrothorax and hydropericardium; acute splenic tumor; small area of bronchopneumonia; glomerulo-nephritis; simple goiter; Meckel's diverticulum.

Autopsy by Dr. MacCallum, December 3, 1898. No. 1208. There was extensive œdema of the face, upper and lower extremities. The peritoneal cavity contained 600 cc. of slightly turbid fluid. Both pleural cavities contained excess of fluid.

The pericardial cavity contained about 200 cc. of a clear fluid in which floated a few flakes of coagulated lymph. Excepting over the right auricle, the serosa was smooth and glossy, here it was noticeably lustreless.

Heart.—Weight 400 grams. The right auricle and ventricle contain firm post-mortem clot. The tricuspid valves are delicate and competent. The pulmonary valves are the seat of a most extensive ulcerative endocarditis, two of its segments being almost completely destroyed, only tags with friable vegetations remaining; the third segment is better preserved and carries on its free margin a soft, friable, rather granular mass measuring $1 \times 2\frac{1}{4}$ cm. Aortic and mitral valves normal.

Spleen weighs 800 grams and measures $23 \times 13 \times 6$ cm. The organ is greatly enlarged and is attached by a few fresh slender adhesions to the body wall and stomach. Capsule generally thickened, but to a moderate degree only. Upon section the spleen is quite soft; color is dark purplish-red;

the trabeculæ are well marked, and the Malpighian bodies are readily visible.

The kidneys are both alike. They are enlarged, weighing together 470 grams and measuring $12\frac{1}{2} \times 7 \times 4\frac{1}{2}$ cm. They are engorged with blood, œdematous and show all the typical signs of acute parenchymatous nephritis.

Bone-marrow of a femur is dark purple-red in color, soft but not diffuent.

The thyroid gland shows a moderate degree of goiter.

Lymph-glands generally are enlarged and firm.

The other organs are either normal or have no bearing in their pathological phenomena upon the special phase of disease under discussion.

MICROSCOPIC EXAMINATION.

Pulmonary Artery Valve.—One of the masses of vegetations examined shows that in its deeper parts it has been quite completely organized, but in its more superficial parts can be observed the presence of a dense mass of hyaline fibrin with a capping of more delicately fibrillated fibrin; more superficially are found small numbers of leucocytes.

The base of the valve is somewhat infiltrated.

Spleen shows great congestion. There is no evident increase in the other tissues. There is no especial accumulation of pigment.

Kidney section presents a few islands of connective tissue of small extent in the cortex. There are accumulations of small round cells about the blood-vessels and adjacent tubules. The tubules are dilated, the epithelium is degenerated and hyaline casts are numerous; many tubules contain leucocytes which sometimes invade the casts. The glomeruli are enlarged and completely fill the capsular space, and show a marked increase in the cells contained within the capillaries, and in some instances a fibrous thickening of the capillary walls is observable.

Bone marrow presents an increase of lymphoid cells. There is no fatty tissue evident.

Lymph-glands show an increase of polymorphonuclear leucocytes and an increase of the endothelium of the sinuses, with swelling of these cells.

BACTERIOLOGICAL REPORT.

At the time of autopsy cultures were made in plain agar, as it was only upon the following day that a suspicion arose of the possibility of gonorrhœal infection and no hydrocele fluid cultures were made. This latter procedure was, however, resorted to later.

The cultures from the vegetations and other sources proved negative on plain agar, excepting those from the lung and peritoneal cavity, which yielded respectively the *Streptococcus pyogenes* and the *Staphylococcus pyogenes albus*.

Within 24 hours of the autopsy cultures were made from the vegetations upon the valve in aseptic fluid agar, but upon examination these proved to be unfit for working out on account of contamination.

Coverslip preparations were made and examined from the vegetations and from the urethra. The former exhibited numerous diplococci sometimes within cells or amongst cell remains, but more often free. Their morphology corresponded closely to that of the gonococcus and they decolorized in Gram's solution. The latter preparation presented no definite micrococci.

CASE 3.—Medical No. 9645. J. H. (colored), æt. 22, was admitted to the hospital upon March 9, 1899, complaining of pain and swelling in the right ankle.

Family history was negative.

Past History.—In childhood he had had mumps, measles and whooping-cough. He never had had rheumatism, typhoid fever, diphtheria nor scarlet fever. He had pneumonia about four years ago. He has no urinary disturbances, and denies gonorrhœa and syphilis, but admits exposure to both.

He does not use alcohol or tobacco.

Present Illness.—One evening four weeks ago he complained of soreness in the right ankle and next morning noticed the region much swollen. Following this he had for several nights chilly sensations and fever accompanied by herpes labialis, but with no night-sweats. He was treated outside for rheumatism.

At the present he complains of aching in all his limbs and especially of pain in the right ankle, which causes him to turn in bed with much difficulty. His ankle joint is swollen.

Physical Examination.—Patient looks ill. There is no cyanosis or herpes. Pressure over femoral artery gave a decided Corrigan impulse, and upon auscultation it gave a pistol-shot sound.

The heart was found much enlarged, the point of maximum impulse being in the fifth interspace 9 cm. from mid-sternal line. There was no thrill present.

Upon auscultation at apex, a loud systolic murmur, traceable far out into the axilla, was heard; likewise a soft blowing diastolic murmur. These could be traced readily upwards and inwards, and could be heard at the aortic and pulmonic areas and along both sternal borders. The second pulmonic sound was relatively accentuated. Pulse shows a fair volume and tension, collapses; rhythm regular and is 26 to the quarter minute.

Lung showed presence of a few coarse râles.

Abdomen and organs negative.

No general glandular enlargement.

Genitalia negative.

Legs show no œdema, no nodes, no scars.

Right ankle is a little swollen, sensitive to pressure, shows no effusion into joint.

March 10th, at midnight, vomiting set in and patient complained of abdominal pain. Pulse small, feeble and rapid. At 8 A. M. his temperature, previously normal, was found to be 100.8°, and the general condition improved considerably over what it had been during the night. But at 8.35 he died suddenly.

Blood Examination.—Leucocytes 55,000 upon day of admission.

Urine.—S. G. 1.011. It showed a few granular casts, epithelial cells and detritus; otherwise it was negative.

Medical bacteriological report upon March 9th proved that the blood culture made was sterile.

ABSTRACT FROM PATHOLOGICAL REPORT.

Autopsy by Dr. Flexner, March 11, 1899. No. 1306.

Anatomical Diagnosis.—Acute endocarditis, perforation of aortic and mitral valves; purulent myocarditis; purulent and hæmorrhagic pericarditis; chronic passive congestion of the lungs; acute splenic tumor; anæmic infarction of spleen and kidneys; acute nephritis; cloudy swelling of viscera.

No œdema present.

Area of pericardium uncovered by lung tissue measures 10 × 10 cm. Upon opening the pericardial sac there is an accumulation of hæmorrhagic and purulent fluid about the great vessels at the base of the heart in the dependent portions of the sac dorsally. In all about 20 cm. of bloody fluid, containing many floating grayish-white purulent masses, can be obtained. The pericardial sac is adherent to the pleural surface of the left lung. The visceral layer of the pericardium is injected; the surface opaque, and there are yellowish adherent masses of fibrin and pus.

Heart weighs 400 grams.

The right and left auricles contain partially decolorized post-mortem clot. The tricuspid and pulmonary artery valves are apparently normal. The heart-wall is lax and the fibers well separated, and the myocardium of left ventricle shows pronounced fatty changes.

The aortic orifice above the valves measures 6 cm.

The Aortic Valve.—The right and middle segments of the valve appear delicate, and the left segment is neither retracted nor thickened, but has been perforated, apparently from below, in that there is a communication just above the base of the valve occupying the width of the right hemisphere of the segment, and measuring about 2 mm. Through this perforation there projects into the sinus of Valsalva a mingled red and white clot, the red portion being soft, the white dense and opaque. This clot almost fills the sinus and connects with a thrombus located upon and within the aortic segment of the mitral valve. This latter thrombus is situated upon the attached portion of the mitral valve, chiefly along the upper half. The valve has suffered a perforation at its base, so that the thrombus protrudes into the cavity of the left auricle. The endocardium of the left auricle above the valve bulges into the auricular cavity over an area 4 cm. sq., its elevation being 2-3 mm. There is no perceptible change in the endocardium itself. Upon incision of this diseased area one enters into a cavity in the substance of the heart-wall, which communicates with the thrombus covering the aortic and mitral valves. This valve [cavity?] contains necrotic and hæmorrhagic material, and at the left edge there is a distinct collection of pus. The cavity meas-

ures $2\frac{1}{2}$ cm. in length and 1 cm. in depth; its walls are infiltrated and firm.

The spleen is enlarged and weighs 400 grams. It has no adhesions. Capsule delicate. In the mid-part of the ventricular surface is a pinkish infarction measuring $2 \times 1\frac{1}{2}$ cm. On section, the organ shows great increase of splenic pulp, consistence is somewhat reduced and the Malpighian corpuscles are visible. The infarction, upon cutting into it, is found to extend inwards for $1\frac{1}{2}$ cm. into the splenic tissue; its consistence is firm.

The liver is congested and cloudy.

Kidneys.—The left one is large. The capsule strips off easily. There is a single anæmic infarction about $\frac{1}{2}$ cm. in diameter, and lies quite superficially. Upon section the cortex is swollen and opaque; the glomeruli are visible and pink in color; striæ are coarse. Thickness of cortex is 8 mm. Resistance is lessened and the organ is œdematous and presents small hæmorrhages in the pelvic mucosa. The right organ is the same in all respects as the left, except for a larger anæmic infarction, measuring 10×12 mm., and a smaller one about the size of a hemp-seed. There are several punctate hæmorrhages in the kidney substance. Combined weight of kidneys is 400 grams.

The Right Ankle-joint.—The periarticular tissues are apparently normal, and the joint contains no excess of fluid, and the synovial membrane is perfectly smooth.

The remaining organs present nothing of significance.

MICROSCOPICAL EXAMINATION.

The heart-muscle is œdematous.

The pericardium is likewise œdematous and thickened, showing an extensive proliferation of blood-vessels constituting a granulation tissue. Upon the surface of this tissue are some remains of epithelium, and here and there a thin, fibrinous deposit. Another section taken through the area of suppuration contains a fibrinous coagulum with many fragments of nuclei; underlying this is a loose granulation tissue infiltrated with leucocytes.

(No sections were made through either of the affected valves, as the heart was preserved as a museum specimen.)

Spleen.—The organ is gorged with blood which spreads apart the splenic elements. One end of the section shows an area of necrosis of splenic tissue sharply marked off by a zone of hæmorrhage with a fibrinous network, inside which is a bluish zone of fragmented nuclei of leucocytes.

Kidney.—Cells of tubules are disintegrated and ragged, showing no nuclei. Some tubules are packed with such desquamated cells.

The glomeruli show no extensive changes. There is no increase of interstitial tissue anywhere.

There are extensive accumulations of polymorphonuclear leucocytes found chiefly in the interstitial tissue, but often, too, in the tubules. Occasional small masses of plasma and round cells are seen in the medullary portions.

There is congestion of the capillary vessels.

BACTERIOLOGICAL REPORT.

Recognizing the possible gonorrhœal origin of the heart lesion, cultures were made upon what at the time was thought to be human serum, as well as upon plain agar, from the vegetations and infarcted areas of spleen and kidney. All endeavors to isolate the gonococcus failed, and this may be explained by the later discovery that by inadvertence ox-blood serum had been used instead of human serum. From the agar-plates the following organisms were isolated:

(a) *Streptococcus pyogenes* from vegetations on aortic and mitral valves, sinus of Valsalva, lung and renal infarct.

(b) *Staphylococcus pyogenes aureus* from vegetations on aortic valve, sinus of Valsalva and lung.

(c) *Bac. proteus vulgaris* from vegetations on mitral valve and sinus of Valsalva.

Cultures from heart's blood, liver, spleen, right ankle-joint and pericardium proved sterile.

Coverslips were from the vegetations on aortic and mitral valves, pericardial fluid, right ankle-joint, infarctions in spleen and kidney. Examination showed that in the vegetations there could be seen large numbers of large diplococci with some single or tetrad forms situated chiefly outside of leucocytes, only scattered polymorphonuclear leucocytes were found containing diplococci or groups of diplococci. The organisms readily decolorized by Gram's method of staining.

The pericardial fluid demonstrated the presence of vast numbers of polymorphonuclear, lesser numbers of large mononuclear and a few small mononuclear leucocytes, amongst which, after very careful searching, could be found a few polymorphonuclear cells containing small groups of diplococci within their protoplasm. These diplococci were larger than ordinary pus cocci, were biscuit-shaped and decolorized by Gram's method. Other coverslip preparations proved negative.

With these statements presented, it is clearly proven that the first case is one of undoubted gonorrhœal origin. But it must be conceded that in the two latter cases the lack of clinical evidence of a recent gonorrhœa, and the failure to demonstrate the presence of gonococci in culture rather weakens the assumption of their being gonococcal in nature.

Yet from the demonstration on coverslip preparations from the material of the valvular vegetations of micrococci, coinciding in all respective non-cultural characteristics with those of standard descriptions of the gonococcus, and, from the peculiar massive formation of the vegetations themselves, we regard it as reasonable that both cases should, without much doubt, be considered as examples of gonorrhœal endocarditis.

DISCUSSION.

A review of the literature since the publication of Thayer & Lazear's article (*Journal of Experimental Medicine*, January, 1899) shows the following cases:

Sears (Medical & Surgical Reports, Boston City Hospital) reports a case in which, following several attacks of gonor-

rhœa, the last attack five months before, the patient, a man aged 23, began to complain of pain in the back, stomach, and limbs, which gradually became more severe. The temperature was elevated from 99.5° F. to 105° F. Examination disclosed a harsh systolic murmur over the pericardium. As the disease progressed, the spleen became enlarged, and finally the pulse irregular and weak with marked cyanosis present. Death occurred on the seventh day after admission to the hospital. Autopsy showed an ulcerative mitral endocarditis, with rupture of the valve segments, infarcts in the left ventricle, spleen and kidneys, and on bacteriological examination a coccus was found quite generally distributed and unlike the ordinary pus cocci. No cultures were taken.

Sears also states that of a hundred and sixty-seven cases of gonorrhœal rheumatism admitted to the Boston City Hospital between the years 1880 and 1897, twenty-five showed cardiac murmurs to which no cause other than gonorrhœa was assignable.

Harbitz (Deutsch. med. Wochenschrift, 1899, XXV, pp. 121-124), in a study of forty-three cases of infectious (*i. e.* caused by organisms, streptococci, gonococci, etc.) endocarditis, found two in which organisms decolorizing by Gram's method, resembling gonococci in other respects, and not growing on the ordinary media (agar, serum, bouillon, gelatin), were found on the affected valves.

Jaccoud, in a clinical lecture on gonorrhœal endocarditis (Journal de Médecine Intern., Paris, 1900, IV, pp. 513, etc.), mentions seventeen cases of gonorrhœal endocarditis, his own and those he has collected for two years, in which the diagnosis was confirmed at autopsy. In four of these gonococci were found on coverslips from the valves, and in the remainder the history pointed clearly to it and autopsy showed ulcerative endocarditis, though no mention is made of what was found bacteriologically. In one of these cases gonococci were found on the valves, and, moreover, the myocardium was altered.

Karageosganz (Eshenedelnik, 1899, No. 46) reports the case of a man, aged 24, who when first seen complained of epididymitis and fever. Examination showed elevation of temperature, anæmia, and a marked systolic murmur over the pericardium. The heart was not enlarged. The spleen was enlarged, and, towards the end of the disease, was four fingers' breadth below the costal margin. The temperature was remittent in character, and there were chills and sweats. The patient had had no disease previously, except intermittent fever. Two years before he contracted gonorrhœa which had never been thoroughly cured, and occasionally showed exacerbations. Death occurred after an illness of one month. Autopsy showed friable yellowish vegetations of the aortic valve, with destruction of the valve segments. No bacteriological examination was made.

Berg (Medical Record, April, 1899) reports the case of a man who, after an attack of gonorrhœa, had involvement of the metacarpo-phalangeal joint of the left thumb, accompanied by chills and elevation of temperature. When first admitted the patient gave evidence of an acute infection, with enlargement of the spleen, but without cardiac involvement. During the course of the disease, however, in which the symptoms became progressively worse, chills, vomiting and finally convulsions, supervening. Signs pointing to pyelo-nephritis and finally endocarditis at the mitral valve, set in, and death followed shortly thereafter. During the course of the disease, repeated examinations of the blood for malarial organisms and several Widal reactions all proved negative.

Cultures from the blood were also taken twice during life, in both instances proving negative.

Autopsy showed acute ulcerative endocarditis of two segments of the aortic valve with vegetations, two small vegeta-

tions on one of the flaps of the mitral valve, acute pyelo-nephritis, acute splenic tumor with one small splenic infarct, acute and chronic parenchymatous nephritis.

Microscopically, diplococci, decolorizing by Gram, were found in the vegetations from the aortic valve, and a few decolorizing diplococci in the fluid from the pelvis of the kidney. No cultures were taken.

The following case is reported by Loeb (Deutsches Archiv für klinische Medizin, 1899, XXV, pp. 411-420). The patient, a man aged forty-one, consulted him for swelling and pain in the right fore-arm. Three weeks before he had had an urethral discharge, but, with the exception of rheumatic pains in the lower extremities, he had otherwise been healthy. During the course of the trouble, which at this time was mild, pleurisy and swelling of the ankle developed, and about two weeks later cardiac signs and symptoms, consisting at first of a soft systolic murmur, but shortly afterwards of loud blowing murmurs at all the cardiac orifices, with both systolic and diastolic murmurs in the mitral area. Higher temperature, chills, and enlargement of the spleen followed and were followed in turn by signs of hypostatic pneumonia and adherent pericardium. Death occurred shortly thereafter. At autopsy the layers of the pericardium were found bound together by friable adhesions. The left heart was somewhat dilated but not hypertrophied. Hard calcareous vegetations, attached to the posterior and right anterior segments of the aortic valve, and projecting into the ventricle, were found. The segments themselves were found thickened and perforated. The remaining valves were unaffected.

The lungs were œdematous but showed no infarcts.

The spleen was enlarged and showed an infarct about the size of a hazelnut.

The kidneys showed change, and there was a small red infarct in the right.

The bladder was negative.

From the vegetations on the affected valve large numbers of diplococci, morphologically similar to gonococci, and decolorizing by Gram's method, were found. Bacteriological examination of the affected synovial sacs and joints and the splenic infarct were negative. No cultures were taken.

A most interesting case is reported by Bjelogolowij (Bolnitche Gazette, Bolkina, January, 1899, No. 4). The patient, a man aged 32, without history of inflammatory rheumatism or other disease except syphilis, was admitted complaining of palpitation and weakness of the heart and swelling of the right testicle, following gonorrhœa of one and one-half months' duration. According to the history the cardiac trouble had come on about two weeks before, and the epididymitis, which it proved to be, was of only a few days' standing.

On physical examination cardiac dulness was found somewhat increased, and at the apex two well-marked murmurs were heard, both being well transmitted. The pulse was collapsing in quality.

Course.—At first the course of the disease was mild, but after several days chills, fevers, sweats, with weakness, vomiting, diarrhœa, pericardial pain and enlargement of the spleen came on, ending finally in the patient's death in collapse.

Autopsy. Anatomical Diagnosis.—Verrucose endocarditis of the tricuspid valve; ulcerative endocarditis of the aortic valve; catarrhal pneumonia; chronic hyperplasia of the spleen; hæmorrhagic infarcts of the spleen; cyanotic induration of the liver; hæmorrhagic infarction of the kidneys; catarrhal colitis; catarrhal enteritis.

Heart.—The pericardium contained several tablespoonfuls of a serous, transparent, yellow fluid. Fibrinous blood-clots were present and a little fluid blood. The walls were pale, of a gray-red color and looked normal. On the upper surface of

the trienspid valve there were several soft, wart-like excrescences, of a reddish color, and about the size of a grain of corn.

The two posterior cusps of the aortic valve were fused, disfigured and thickened with yellowish excrescences, which were covered on the surface with a friable and readily removable mass. The sinuses of Valsalva were dilated. The right cusp had a perforation the size of a goose-quill, filled with a bloody, fibrinous clot.

The mitral valve was normal.

Lungs.—Fibrinous pleurisy was present. Lungs otherwise negative save for a broncho-pneumonia at base.

Spleen.—Double its normal size, dark-colored, dense, trabeculae well marked, and presenting on the lower aspect at the edges a hæmorrhagic infarct the size of a hazelnut.

Liver.—Normal, yellowish-red color, full-blooded.

Kidneys.—Large, capsules strip with difficulty; the cortical layer of each kidney thickened and contains a discolored hæmorrhagic infarct the size of a pea. The tissue is darker than normal and there is pus present in the pelvis of each kidney.

The mucosa of the bladder, beyond being pale, seemed normal.

The stomach and intestines were normal save for a catarrhal colitis.

The knee and ankle joints showed no change.

Phimosis was present. From the fossa navicularis a small drop of pus was expressed.

The testicles were without apparent change.

During life examination of the blood was made in the following ways with these results:

1. Slide of blood, stained with methylene-blue and eosin, showed apparently diplococci, but this is doubtful.

2. A small drop of blood from the finger planted on gelatin and peptone-agar gave no growth.

3. One cc. of blood was obtained, under aseptic precautions, from the vein at the elbow, and three plates, consisting of two-thirds glycerin-agar and one-third hydrocele fluid, were successively inoculated.

After forty-eight hours over twenty whitish, punctate colonies developed on the three plates. In some of these a darker center was noticed.

Microscopically, diplococci, resembling gonococci and decolorizing by Gram, were found.

Transplantation on gelatin-agar and on bouillon gave negative results.

Transplantation on an hydrocele-agar slant gave a slowly developing, beautiful growth, resembling that of the gonococcus in all respects, and proving the presence of gonococci in pure culture in the blood.

After death bacteriological examination gave the following results:

1. About twenty-four hours after death culture from the heart's blood made on hydrocele-agar gave negative result.

2. Tubes of agar, bouillon, gelatin and hydrocele-pepton-glycerine-agar were inoculated with material obtained from the vegetations of the aortic valve; all with negative result.

3. Microscopical examination of the material from the vegetations of the aortic valve showed, however, diplococci completely identical with those found during life in the blood. These occurred both intracellular and extracellular, and decolorized by Gram.

4. No organisms were found microscopically on section of the splenic infarct.

NOTE.—Since the foregoing article has gone to press, a fourth case has come under our notice in the Pathological Laboratory.

Autopsy No. 1630 —. There was a clear clinical history of an acute gonorrhœal urethritis, for which the patient had come to the dispensary for treatment. At the end of a week he disappeared, but returned in three months complaining of having had rheumatism of the joints, and pains in the chest and feeling generally unwell. He was at once admitted to the hospital under Dr. Osler's care, where his heart was found to be seriously involved. He died that night.

The autopsy showed an acute ulcerative endocarditis of the aortic valve, similar in character to that mentioned in Cases II and III. In coverslip preparations made from the vegetations micrococci were found having all the characteristics, morphologically and tinctorially, of Neisser's gonococcus. Owing to an unavoidable lapse of time and to over-much handling of the heart, cultures proved an absolute failure on account of resulting contamination.

N. MacL. H.

W. M. D.

AN EXPERIMENTAL STUDY CONCERNING THE RELATION WHICH THE PROSTATE GLAND BEARS TO THE FECUNDATIVE POWER OF THE SPERMATIC FLUID.

BY GEORGE WALKER, M. D.,

Instructor in Surgery, Johns Hopkins University.

In order to elucidate more clearly the connection which the prostate gland holds to fertilization, I have instituted a series of experiments in which the gland in white rats was excised in part and in whole, and its effects on fecundity noted.

Steinach, in a series of investigations made to determine the function of the seminal vesicles, found that by an excision of them the breeding property was reduced about one-half. When both prostate and vesicles were removed, it was brought down to nil. He did not excise the prostate gland alone, and could therefore adduce no proof as to the part it played.

Rats were selected on account of the ease with which the gland could be removed, and also from the minimum amount of danger of injuring the seminal ducts; the two being in rodents quite distinct, and not connected. The gland consists of four, or sometimes six, distinct lobes; the two anterior ones are very much larger than the others; are pear-shaped, and stand well up and away from the urethra, being held by a fascia connected with the bladder. They communicate with the urethra by several small ducts which empty into the roof of the lumen just in front of the vesicle neck. The posterior lobes are somewhat triangular in shape, are more closely connected with the urethra, and

are very much smaller and flatter, forming about one-fourth of the whole gland. They extend slightly around the ejaculatory ducts, and well up on the side of the urethra. The two lateral lobes are only occasionally present, and seem to be developed from the posterior ones. A second glandular substance is connected with the inner side of the seminal vesicles, and presents the same macroscopic appearance as does the prostate; but on microscopic section it is shown to be a structure similar to that of the vesicles.

The excision of the glands was done thus: The animals were etherized, the abdominal wall was carefully shaved and cleansed, and an incision made in the median line. This brought the anterior lobes into view, and by gently pulling the bladder forward and upward, they could very plainly be seen. They were very carefully separated from the bladder and from each other; a ligature was thrown around each, near the urethra, and both lobes excised; the posterior ones were exposed by pulling the bladder and seminal vesicles over the pubes; they were then very carefully separated from the surrounding structures and teased by a pair of small forceps from their connection with the urethra. This occasioned only slight bleeding, which soon ceased without a ligature. The abdomen was closed by interrupted silk sutures, the skin in the same manner, and the wound dressed with cotton and collodion. The animals usually made a rapid recovery, and appeared very lively on the following day.

The rats selected for operation were full grown, well developed, and in good physical condition. In several series the two anterior lobes were excised, and the effect on procreation noted. In the other series, all of the gland was removed, and the result also recorded.

The first series consisted of seven pairs; these were mated, and the number in the litter carefully noted. The two anterior lobes were then removed, and after sufficient recovery they were again mated.

Pair No. 1. Mated July 10th. Five weeks later the female gave birth to eight young; anterior lobes excised, and after recovery again mated August 22d; September 15th, a litter of eight was found.

Pair No. 2. Previously mated, and gave birth to ten young; two anterior lobes removed, and second mating August 24th. After two months, negative result.

Pair No. 3. Previously mated; five young. Anterior lobes excised and paired August 15th. Six weeks afterwards, four young.

Pair No. 4. Previously mated; eight young; removal of anterior lobes, and mated August 18th; after seven weeks, two young.

Pair No. 5. Previously mated; seven young. Anterior lobes excised, and second mating August 21st; after seven weeks, eight young.

Pair No. 6. Previously mated; eight young; anterior lobes excised, and mated second time August 23d; negative result.

Pair No. 7. Previous mating resulted in eight young;

removal of anterior lobes; second mating August 30th; negative result.

From the above it is seen that in two pairs the breeding was normal; in two others the number was reduced to two in one case, and to four in the other, while in the remaining three the result was entirely negative.

A second series of fifteen pairs was taken; no previous mating, however, being done, as it had been ascertained by watching several other series that rats are fertile in nearly every instance. As in the preceding series, only the anterior lobes were removed; after complete recovery they were paired with the females.

Pair No. 1. Positive result after five weeks; eight young.

Pair No. 2. Positive result after six weeks; seven young.

Pair No. 3. Positive result after six weeks; eight young.

Pair No. 4. Positive result after five weeks; five young.

Pair No. 5. Positive result after eight weeks; ten young.

Pair No. 6. Positive result after nine weeks; eight young.

Pair No. 7. Positive result after four weeks; six young.

Pair No. 8. Positive result after six weeks; seven young.

Pair No. 9. Positive result after five weeks; five young.

Pair No. 10. Negative result after three months and twenty-five days.

Pair No. 11. Negative result after three months and twenty-five days.

Pair No. 12. Negative result after three months and twenty-five days.

Pair No. 13. Negative result after three months and twenty-five days.

Pair No. 14. Negative result after three months and twenty-five days.

Pair No. 15. Negative result after three months and twenty-five days.

Afterwards the males were killed, and the seat of excision examined. In three of the fertile ones it could be seen that a small amount of the anterior lobes had been left, while in the others it had all apparently been taken away. In the ones which had proved unfertile, there was no part of the anterior portion present. In quite a number of them, and most notably marked in the ones which had proved fertile, the posterior lobe had increased in size. In the negative ones no such increase in size was apparent.

A third series of animals was selected and mated before operation. The ones which bred were chosen for the excision of the gland. At the first operation only the anterior lobes were removed; they were again mated, and the fertile ones selected and subjected to a second operation in which all of the gland was taken away. The result is as follows:

Pair No. 1. Mated before operation; bred five. March 1st, removal of anterior lobes. Second mating March 5th. April 10th, bred three. April 12th, removal of the remaining gland; again mated; negative result.

Pair No. 2. Previous to operation bred eight; removal anterior lobes March 1st; mated March 4th; negative result. Second operation, entire removal April 10th; negative result.

Pair No. 3. Before operation bred four. First operation February 18th; mated March 3d. April 3d, bred seven. Second operation April 24th; entire removal. Mated April 26th; negative result.

Pair No. 4. Before operation bred seven; operation, removal anterior lobes March 1st; mated March 3d; April 22d, bred four. Complete removal April 24th; mated April 26th. After six weeks, positive result; bred six.

Pair No. 5. Before operation bred six; removal anterior lobes March 1st; mated March 3d; April 15, bred six. Second operation May 7th; complete removal; negative result.

In the above series, four out of the five were fertile after the first operation; number two being negative after the first and after the second. In two the number was normal, but in the remaining two pairs, the number was decreased in one case from five to three, and in the other from seven to four. In one pair, however, number three, it was increased from four to seven. After the second operation, four out of the five were sterile, only one bred.

The autopsies showed in the four barren ones that the gland had been entirely removed, whereas in the fertile ones, about three-fourths of the posterior lobes had not been excised.

In order to determine whether the seminal ducts had been injured during operation, and thus had prevented the outflow of the seminal fluid, a careful examination of both orifices and canals was made; they were found in each instance to be patent; moreover, on gently squeezing the seminal vesicles the secretion freely oozed through the orifices, and on stripping the vasa deferentia, the secretion freely exuded from the openings. The fluids thus obtained were examined microscopically and found to contain spermatozoa.

A fourth series of eleven pairs was selected, and the entire gland removed at one sitting. These, after recovery, were mated, with the result below recorded. It should be noted that the females had been kept for a long time separate, so that it was made sure that no fertilization was present.

Pair No. 1. After sufficient length of time proved negative.

Pair No. 2. Negative.

Pair No. 3. Negative.

Pair No. 4. Negative.

Pair No. 5. Negative.

Pair No. 6. Negative.

Pair No. 7. Negative.

Pair No. 8. Negative.

Pair No. 9. After six weeks, positive result; three young.

Pair No. 10. After seven weeks, two young.

Pair No. 11. After five weeks, five young.

It will thus be seen that in the eleven cases, eight were entirely negative, and in the remaining three, there was not a full litter in any instance; five being the nearest approach to it; in the other two the litter being two and three respectively.

The autopsies of Nos. 1, 2, 3, 4, 5 and 6, showed a com-

plete removal of the gland; No. 7 presented a small piece of the lateral lobe; No. 8 showed only a slight trace of the left lobe; No. 9 showed fully three-fourths of the posterior lobes present, and a moderately sized stump of the anterior ones; in No. 10 there was found a large lateral lobe which had not been excised. In No. 11, although a positive result was obtained, there was apparently no gland left, either posterior or anterior. This last case was the only example in the whole series in which the male had proved fertile with no portion of the gland remaining.

The examinations proved that in most of the negative pairs there had been a complete removal of the gland; in two cases, however, some of it was present, while in the fertile ones, two presented large remnants of the gland which had failed to be excised; in one instance, all had apparently been removed. A similar examination as to the patency of the seminal ducts was made, and in only one instance was an occlusion found, and in that it was in only one duct. The others were perfectly open, and emitted their secretion.

The sexual desire and capacity of the rats were carefully noted both in those in which a partial excision, and in those in which a complete excision had been done. The examination was made by carefully watching them for some time each day after they were mated, subsequent to the operation. In every instance, the males were as sexually active after the operation as before; and in no instance was the capacity diminished.

The animals in which a complete removal of the prostate gland had been done were kept from four to seven months after the operation in order to ascertain whether any effect had been produced on the testes by the removal of the gland. At the end of this time the animals were killed with chloroform, and the organs carefully removed and examined. In every instance they were of normal size, of natural consistency, and in no way did they differ from the usual type. They were preserved in Zenker's fluid, and the subsequent microscopic sections did not reveal any changes.

In order to determine whether any effect was produced in the development of the testes by a very early removal of the prostate gland, I selected a certain number of young and healthy males, just at the age when the gland was beginning to develop; another series of about the same age being kept as controls. The prostate glands in the first number were entirely excised; the animals were kept for nearly six months, by which time they were thoroughly grown. They were then killed, and the testes upon examination were found to have developed normally; and they presented the same appearance and feel as were present in the other series of rats which were kept as controls. These were also examined microscopically, and no difference was found in them. The seat of the operation was examined; in one there had been a partial development of the gland; in the others no trace of it was discernible.

SUMMARY.

First series of seven pairs; anterior lobes excised; two bred normally, two had small litters, two were negative.

Series No. 2. Fifteen pairs; anterior lobes removed; nine bred normally, five proved negative, one escaped.

Series No. 3. Five pairs; after first operation, removal of anterior lobes; four out of five bred normally; one was negative. After a second operation where complete removal was done, one bred normally, four were negative.

Series No. 4. Eleven pairs; complete removal of the gland at one sitting; eight were negative, three had small litters; none positive.

Series No. 5. Prostate gland removed in early life, did not have any effect on the subsequent development of the testes.

CONCLUSIONS.

From the above experiments, the following conclusions can safely be drawn:

First. That a removal of the anterior lobes of the prostate gland in rats has no effect on breeding; but in a certain number it diminishes the fecundating power; and in a few it is destroyed entirely.

Second. Complete excision has a very marked effect on fecundity, reducing it to almost nil when the gland is entirely removed.

Third. Partial or complete removal of the prostate has no effect upon the sexual desire and capacity.

Fourth. Complete removal of the gland in the adult animal has no effect on the histological structure of the testicles. Complete removal of the prostate in the young animal has no effect upon the subsequent development of the testes.

SUMMARIES OR TITLES OF PAPERS BY MEMBERS OF THE HOSPITAL AND MEDICAL SCHOOL STAFF APPEARING ELSEWHERE THAN IN THE BULLETIN.

CHARLES RUSSELL BARDEEN, M. D. Casto-Vertebral Variation in Man.—*Anatomischer Anzeiger*, November 7, 1900.

SIMON FLEXNER, M. D. Nature and Distribution of the New Tissue in Cirrhosis of the Liver (Preliminary Communication).—*Proceedings of the Pathological Society of Philadelphia*, November, 1900.

WILLIAM OSLER, M. D. An Address on John Locke as a Physician.—*Lancet*, London, October 20, 1900.

HOWARD A. KELLY, M. D. A Rapid and Simple Operation for Gall-Stones Found by Exploring the Abdomen in the Course of a Lower Abdominal Operation.—*Medical News*, December 22, 1900.

HENRY J. BERKLEY, M. D. Clinical Cases. VII. The Pathology of Chronic Alcoholism.—*The American Journal of Insanity*, January, 1901

FURTHER OBSERVATIONS ON EPINEPHRIN.

BY JOHN J. ABEL, M. D.,

Professor of Pharmacology, Johns Hopkins University.

Shortly after the publication of my last paper on epinephrin,¹ I began to try simpler methods for the isolation of this substance, methods which should avoid the process of benzoating and the subsequent hydrolysis in the autoclave. Although the highly active bisulphate that was secured by these simpler methods was considerably contaminated with cholin and with compounds of the xanthin series, these attempts nevertheless taught me that the autoclave product as formerly described differs in several important particulars from that obtained without benzoating or subsequent hydrolysis. The latter product, which I might term unaltered or native epinephrin, is not precipitated by ammonia and fails to give many of the alkaloidal reactions which are characteristic of the autoclave product.

At first glance it might appear that the epinephrin hitherto described by me was a mixture of two different substances, one of which is precipitable by ammonia; the other, a physio-

logically active, pyrocatechin-like substance, not possessing this property; and this is in fact the view taken by v. Fürth² in a paper in which he comments on my results. This author, using a modification of the earlier methods of Holm³ and Krukenberg⁴ precipitates epinephrin with ammonia and a lead or zinc solution, suspends the resulting precipitate in methyl alcohol and decomposes it with concentrated sulphuric acid.

In this way he obtains a methyl-alcohol solution of a sulphate which has not been subjected to hydrolysis, and since it differs in several important particulars from epinephrin as described by me, he concludes that we are dealing with two different substances. He considers the term epinephrin to be applicable to a substance that is physiologically inactive, precipitable by ammonia, devoid of chromogenic properties, incapable of reducing silver nitrate or of forming a compound

¹ *Zeitschr. f. physiol. Chem.*, Bd. xxviii, s. 318.

² *Zeitschr. f. physiol. Chem.*, Bd. xxix, s. 105.

³ *Journ. f. pract. Chemie*, Bd. c (1867), s. 150.

⁴ *Virchow's Archiv*, Bd. ci (1885), s. 542.

with ferrie chloride, while he applies the name suprarenin to the well known chromogen or physiologically active substance which in its native condition is non-precipitable by ammonia, reduces silver nitrate, yields an iron compound of specific qualities, fails to give a series of alkaloidal reactions characteristic of hydrolyzed epinephrin, and on fusion with potassium hydrate yields no odor of indol or skatol. Such, in brief, according to v. Fürth, are the main characteristics of what he calls two different substances.

I propose in this paper to take up the main points presented by v. Fürth and I hope to show that differences of method are alone responsible for the variations he has noted. What v. Fürth calls suprarenin is native or unaltered epinephrin.

I. PRECIPITATION BY AMMONIA.

Epinephrin obtained by hydrolyzing its benzoyl compound is precipitable from an aqueous solution by ammonia in the form of yellowish-white floes which rapidly darken on exposure to the air and which are physiologically inactive. And here it may be remarked that complete precipitation of a salt of epinephrin is attended with some difficulty. The fractional method must be used in order to avoid an excess of ammonia, and toward the end of the operation, when only a little of the chromogenic substance remains, it is necessary to concentrate the solution with the help of the vacuum desiccator before the final precipitation is made. The various precipitates may be washed with ice-water, although it must be borne in mind that prolonged washing will dissolve almost all of the flocculent precipitate with the exception of a small amount of a dark insoluble residue which has become oxidized by long exposure to the air. When the fractional precipitation has been properly conducted the final filtrate from a solution of epinephrin bisulphate, for example, will contain nothing but ammonium sulphate, while on the various filters will be found all of the chromogenic substance.

Now, epinephrin, the chromogenic substance of the suprarenal gland, whether isolated by v. Fürth's or any other method that does not involve hydrolytic treatment, becomes immediately precipitable by ammonia as soon as such hydrolytic treatment is applied. Proof for this statement is found in the following facts:

1. The iron compound of "suprarenin" was prepared according to v. Fürth's method, which I consider a distinct contribution to our knowledge of the subject. His directions were followed with the exception that the compound was redissolved and reprecipitated out of acidulated methyl alcohol in order to remove as far as possible impurities that might be present. I then made benzoyl and acetyl epinephrin from this iron compound, and on saponifying these derivatives in the autoclave, I found that the resulting solutions yielded flocculent, inactive epinephrin on the addition of ammonia; in other words, they behaved exactly like compounds of the same name formerly described by me.

2. By cautiously adding ammonia to the methyl alcohol solution from which v. Fürth prepares his iron compound, I removed all excess of sulphuric acid and then drove off the

methyl alcohol in the water bath. The residue was now taken up in water, filtered and heated in the autoclave for two hours in the presence of a little sulphuric acid and under a pressure of four atmospheres. The solution, which at first gave no precipitate with ammonia, now yielded an abundant flocculent precipitate on the addition of this reagent. Furthermore, I dissolved the iron compound in methyl alcohol containing a little acetic acid and removed the iron by repeated treatment with hydrogen sulphide. After evaporation of the methyl alcohol the residue was taken up in water, a little dilute sulphuric acid was added and this solution was hydrolyzed as before. Here again, the same result was obtained. The solution, which before treatment in the autoclave gave no precipitate with ammonia, now yielded epinephrin in abundance.

3. It might be asserted that the above facts are capable of another interpretation, that the substance which on hydrolysis yields this flocculent precipitate is not the chromogenic substance of the suprarenal capsule but an entirely different body which on precipitation drags down the chromogenic substance with it; that it is in fact merely present in v. Fürth's iron compound as an impurity. But my experiments with the active bisulphate of epinephrin, which can be converted quantitatively into this flocculent substance (barring small losses by conversion through oxidation into an insoluble form), fully prove that a separation of this body into a chromogenic and a non-chromogenic substance is impossible. It is itself, as stated in my earlier papers, an inactive modification of the active substance of the suprarenal gland. A further proof of this assertion is seen in the following: A chemist in the employ of one of our manufacturing firms has recently sent me about 1-10 of a gram of a micro-crystalline compound derived from the suprarenal gland that possessed a high degree of physiological activity and gave all the specific reactions of the native non-hydrolyzed form of the active principle. The method of its manufacture has not been made public and I have not as yet determined whether the compound represents the free base itself or some crystalline derivative.

This compound, which dissolves only sparingly in cold water, also fails to give a precipitate with ammonia unless subjected to treatment in the autoclave, behaving, therefore, like all specimens of the chromogen thus far isolated.

In short, it is an inherent property of the active principle of the suprarenal gland, prepared by whatever method, to fall out in the form of a flocculent, physiologically inactive precipitate on the addition of ammonia after previous treatment in the autoclave.

It is not surprising that v. Fürth should have failed to note this property of epinephrin inasmuch as he did not test any of my compounds as made by saponification of the benzoyl derivative, in respect to their precipitability by ammonia, but applied this test only to solutions obtained by decomposing his ammoniacal lead on ammoniacal zinc precipitates. The substance obtained by him from these solutions on the addition of ammonia is not epinephrin; it is either some de-

generate product of it or an entirely different substance. His observation that the active principle in its native state is not precipitable by ammonia is, however, entirely correct.

II. ON THE IRON COMPOUND OF EPINEPHRIN.

Now that it has been shown that some of the properties of epinephrin, as heretofore described, are not inherent in the native substance but are developed by chemical manipulation, it is of interest to inquire into the behavior of its two chief modifications toward iron salts.

As before stated, v. Fürth has shown that a solution of the active principle in methyl alcohol yields a highly active precipitate on the addition of ferric chloride and ammonia, and that the addition of ferric chloride to a dilute aqueous solution containing a little acid gives a bright green color, while if the solution is alkaline, a carmine red color is the result.

Up to this time no analyses of this iron compound or of its derivatives have been given, nor are we informed whether its iron content varies on re-solution and re-precipitation, nor how far variability in this respect is affected by different modes of manipulation.

This author also appears to believe that the salts of epinephrin described in my previous papers are incapable of yielding an iron compound except as the chromogen is present as an impurity. But the experiments presently to be described show that epinephrin bisulphate is quantitatively convertible into an iron compound indistinguishable in appearance and chemical reactions from that described by v. Fürth, although differing in two respects from his compound: first, in that it can be precipitated directly from an acidulated aqueous solution of epinephrin, and second, that it is physiologically inactive. These differences, however, like others already alluded to, are due solely to differences in previous manipulation; in short, the conditions here are the same as in the case of the precipitation by ammonia, for if the methyl-alcohol solution from which v. Fürth derives his iron compound be taken and the methyl alcohol expelled, the residue dissolved in water, acidulated with a little dilute sulphuric acid and treated in the autoclave as already described, a transformation into what I have hitherto called epinephrin will be found to have occurred.

After removal from the autoclave the solution still possesses a high degree of physiological activity, but the addition of ferric chloride and ammonia now yields a precipitate, the iron compound of epinephrin, which is physiologically inactive. Here, too, the hydrolytic action of the autoclave is responsible for an inactive form of the iron compound, capable of precipitation out of acidulated aqueous solutions of the active principle.

CONVERSION OF EPINEPHRIN BISULPHATE INTO AN IRON COMPOUND.

The following experiment was made with 1.197 grams of pure epinephrin bisulphate, another portion of which had served as the source of the phenylcarbamic di-ester of epi-

nephrin described by me in an earlier paper.⁵ The salt was dissolved in very dilute sulphuric acid, and ammonia was cautiously added until about two-thirds of the epinephrin was precipitated in two fractions in the form of yellowish-white flocks. These were repeatedly washed with ice water and the washings were added to the original filtrates. The flocculent precipitates were now separately dissolved in very dilute sulphuric acid and converted into an iron compound by the addition of ferric chloride and the subsequent addition of ammonia to very near the neutral point.

These precipitates were repeatedly washed by sedimentation in tall cylinders until the ammonium sulphate was entirely removed.

The compound was then redissolved in dilute sulphuric acid, reprecipitated with ammonia and washed as before, collected on a filter and dried over sulphuric acid.

The filtrates from the precipitations by ammonia together with the washings were also converted into the iron compound, which, after being washed in a tall cylinder by sedimentation, was redissolved in very dilute sulphuric acid, reprecipitated by ammonia and washed till all traces of sulphuric acid had disappeared.

In this connection it may be remarked that the washing of the iron compound as above described until it is free from ammonium sulphate and sulphuric acid is accomplished with difficulty. Large quantities of water are required and the amount of the iron compound which remains in solution in the supernatant fluids depends of course upon the reaction of these fluids. This reaction, I may remark, is difficult to maintain at the same level in the several cases. Usually the wash fluids were colorless, but even then the addition of ammonia caused a farther precipitation of the iron compound. It is to be noted, also, that the iron content of the compound here considered varies with the conditions of its precipitation. Thus, if the iron content of a given fraction is 8.50%, that precipitated from its washings may be as high as 12.62%, or even higher, and this same variability is met with if the portion on the filter is redissolved and reprecipitated. Whether this variability also attaches to the physiologically active iron compound obtained by the use of methyl alcohol has not yet been determined.

Briefly stated, the results of the above experiments are as follows: 1.197 grams of epinephrin bisulphate made from the benzoyl compound were treated with ammonia until the larger portion of the epinephrin was precipitated; this was washed with cold water and the washings added to the original filtrates. Both the flocculent free epinephrin and that which still remained as a bisulphate in the filtrates were converted into an iron compound. According to v. Fürth, only the filtrate and the washings from the free epinephrin could yield an iron compound. Yet after all the manipulations above described the following fractions of this iron compound were obtained:

⁵ Amer. Journ. of Physiol., vol. iii, 1899-1900, No. 8, p. XVII.

From epinephrin, Precipitate I.	From epinephrin, Precipitate II.	From the filtrates from Precipitates I and II.
0.1412 gram.	0.2845 gram.	0.2438 gram.

From the washings of these precipitates further amounts of the iron compound were obtained and in relatively the same proportion in each case. These additional fractions, together with what was recovered from filter papers, cylinders and funnels, brought the total amount of the iron compound obtained up to 0.9242 gram. A small quantity, amounting to perhaps 0.02 gram was further precipitated from the washings of the last fraction and was not taken into consideration.

The object of the above experiment was to learn whether this compound can be as easily made from flocculent, inactive epinephrin as from its filtrates, but the fact which incidentally appeared, that notwithstanding the many manipulations involved, so large an amount as 0.9242 gram of an iron compound was obtained from the above-mentioned quantity of bisulphate, fairly warrants the statement that epinephrin bisulphate is quantitatively convertible into an iron compound.

In the case of the iron compound from epinephrin, Precipitate II, and from the filtrates from epinephrin, Precipitates I and II, like conditions of precipitation were maintained both in respect to the amounts of the reagents employed and the reaction of the wash fluids, with the result that the iron content of the two fractions was nearly the same. This is shown in the following table:

Iron compound from epinephrin, Precipitate II.	Iron compound from filtrates from epinephrin, Precipitates I and II.
0.1105 gm. burned on an ashless filter left 0.014 gm. $\text{Fe}_2\text{O}_3 =$ 8.87 per cent Fe.	0.0965 gm. burned on an ashless filter left 0.0122 gm. $\text{Fe}_2\text{O}_3 =$ 8.85 per cent Fe.
0.174 gm. burned in a current of oxygen, left 0.021 gm. $\text{Fe}_2\text{O}_3 =$ 8.44 Fe.	0.1473 gm. burned in a current of oxygen, left 0.0189 gm. $\text{Fe}_2\text{O}_3 =$ 8.96 per cent Fe.

The carbon and hydrogen content of the two fractions was also in fairly close agreement, but the analyses are reserved for consideration in a later paper in which I hope to give a fuller comparison of this compound and that made by v. Fürth in the manner already described. A single analysis of a specimen of the latter compound was made and it was found to contain 12.8 per cent of iron.

This higher iron content unaccompanied by other data affords no basis of comparison between the two substances; for, as we have seen, a fraction of my iron compound which contains 8.5 per cent of iron may by chemical manipulation have its iron content raised to over 12 per cent.

In conclusion, then, it may be stated that an active salt of epinephrin made by saponification from its benzoyl compound is convertible into an iron compound, both in methyl alcohol and in aqueous solution.

When made from an aqueous solution this iron compound is physiologically inactive, also less soluble in dilute acetic acid than v. Fürth's compound, but in respect to its chemical reactions it is indistinguishable from his compound.

By benzoating the iron compound of v. Fürth, trial experi-

ments have shown me, that the entire series of derivatives formerly described by me may be obtained. From it I have also made the acetyl compound and by decomposing it in the autoclave I have obtained an active bisulphate indistinguishable in appearance and reactions from that formerly described by me.

Our compounds also agree in yielding, on the addition of moderately strong alkali, the volatile base of a coniinepiperidine-like odor so often noted in my previous papers.

III. OTHER EFFECTS OF TREATMENT IN THE AUTOCLAVE.

V. Fürth has also stated that the active principle of the gland as contained in the fluids prepared from his lead or zinc precipitates, yields no precipitates on the addition of certain alkaloidal reagents, as picric, phosphotungstic or tannic acid, iodine in potassium iodide or concentrated solution of zinc chloride.

It is, however, easy to prove that here, too, as in the instances relating to precipitability with ammonia and with ferric chloride, we are dealing with characteristics which only require appropriate treatment for their development. If the iron compound prepared according to the directions of v. Fürth is converted into the acetyl derivative and this is saponified in the autoclave, a solution is obtained from which the epinephrin bisulphate formerly described by me can be prepared without difficulty. Aqueous solutions of this salt readily give precipitates with the above-named alkaloidal reagents, while solutions which are derived from the material from which v. Fürth's iron compound is prepared, that is to say, from material which has not been exposed to hydrolysis, fail to give precipitates with these reagents.

A further instance of this behavior is furnished by the compound already alluded to as having been sent to me by the chemist of one of our manufacturing firms. Before treatment in the autoclave with dilute sulphuric acid this substance also yields no precipitate with such alkaloidal reagents as picric acid, phosphotungstic acid, iodine chloride or iodine in potassium chloride, but after such treatment a prompt precipitation occurs on the addition of these reagents.

IV. SKATOL: A DECOMPOSITION PRODUCT OF EPINEPHRIN.

I have stated in previous papers that on fusing the chromogen of the gland with powdered potassium hydrate and then diluting with water the penetrating odor of skatol arises from the solution. When this solution of the fusion products was shaken with ether and the ether allowed to evaporate, little globules remained, having an intensely faecal odor and giving the characteristic reactions of skatol with sufficient definiteness to warrant the belief that this substance is a decomposition product of the active principle under the conditions specified.

V. Fürth has failed to substantiate my statements in this particular, but the tests which I have made with the acetyl compound prepared directly from his own iron compound, as also with a specimen of epinephrin bisulphate prepared

from this acetyl derivative have still further convinced me that my statements were correct. In order to get olfactory evidence of the presence of skatol, it is only necessary to smelt about 0.1 gram of either of these compounds in a cautious manner with an appropriate amount of powdered potassium hydrate, the two reagents being spread out on the bottom of an Erlenmeyer flask, then to dilute with water, shake with ether, and evaporate the ether out of a Drechsel wash bottle with the help of a suction pump. The water contained in the ether is left behind as ice and the low temperature produced is an effectual bar to the complete escape of the skatol. On opening the wash bottle after the removal of the ether one obtains sufficient proof that skatol is present from its characteristic odor.

V. ANALYTICAL CONSIDERATIONS.

It would now be in order to give analytical data to illustrate the changes that occur in the autoclave and to show what relation obtains in respect to elementary composition between the autoclave product and its less manipulated, physiologically more active counterparts. But an accident that happened to me in my laboratory in the early days of December and which for nearly three months kept me from my laboratory has made more than an introductory discussion of this point impossible.

It would appear that the simplest method of arriving at a conclusion in regard to the extent of the analytical differences existing between epinephrin as made by the autoclave method and that made by avoiding this treatment, would be to analyze the acetyl derivative when made from v. Fürth's iron compound. The direct conversion of this iron compound into its acetyl derivative contends with the difficulty of purifying and washing the former substance in consequence of its amorphous character, and is also open to the suspicion that secondary changes, such as oxidation, may occur in the process of acetylizing. I have nevertheless converted this iron compound into its acetyl derivative, without first removing the iron. Preliminary analyses have shown that its nitrogen content varies from 4.18 to 4.28 per cent. My empirical formula, for triacetyl epinephrin as made by the autoclave method, calls for 3.31 per cent N. In the above instances the nitrogen content was determined by the method of Kjeldahl, and the observed deviation from the theoretical requirements are too large to bring the acetyl compound now under consideration into a simple relation with that formerly described by me.

It may be remarked in passing that the observed results vary still more widely from those found by v. Fürth, who gives 5.71 per cent as the average nitrogen content of his acetyl compound, while the theoretical requirement is either

5.81 or 5.86 per cent, according as the one or the other of his assumptions that the active principle is tetrahydrodioxypyridin or dihydrodioxypyridin is made the basis for the empirical formula.

At the present moment it is impossible to express, in analytical terms, the differences that exist between the epinephrin of my former papers and the somewhat less altered, native principle. Their qualitative differences and resemblances have been pointed out in this paper. While it is perhaps unwise to anticipate the results of future researches, I would suggest that one or more of the following chemical changes may possibly account for the differences that have been noted: 1. The saponification of the benzoyl derivative may not be a complete one; one benzoyl group may have been retained, in which case my epinephrin would represent the monobenzoyl derivative of the native principle. 2. Inasmuch as treatment in the autoclave of every form of the active principle, no matter how prepared, leads to the appearance of new properties, it is in order to ask whether the entrance of one or more molecules of water into the compound, or the loss of an atom of nitrogen in the form of ammonia or a combination of these two alterations, will not be found to lie at the bottom of the whole difficulty. In case one or both of these changes take place, they would of course also occur in the case assumed under 1. 3. It is also possible that the autoclave is responsible for a doubling of the original molecule after previous elimination of water and also of nitrogen in the form of ammonia or of a simple amine.

These and other points will constitute the subject matter of a future communication. The methods that have hitherto been employed by me have served their purpose in giving us unstable but characteristic derivatives of the native principle. These have retained a high degree of physiological activity and give all the known reactions of the native product, but they show, in addition to these, certain new reactions, such as precipitability by ammonia and by alkaloidal reagents.

In conclusion I would state that the autoclave is also responsible for a decrease in the physiological activity of the compound. This is shown by the data recently obtained by Prof. Reid Hunt⁶ with a specimen of unaltered epinephrin bisulphate, which was prepared from v. Fürth's lead precipitate, by removal of the lead and subsequent fractional precipitation. Other methods of isolation in which also the use of the autoclave plays no part are now in progress in my laboratory, and detailed statements as to the composition and physiological activity of the resulting products will follow later.

⁶ Amer. Jour. of Physiol., vol. v, No. 2, p. VII.

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In the methods of instruction especial emphasis is laid upon practical work in the Laboratories and in the Dispensary and Wards of the Hospital. While the aim of the School is primarily to train practitioners of medicine and surgery, it is recognized that the medical art should rest upon a suitable preliminary education and upon thorough training in the medical sciences. The first two years of the course are devoted mainly to practical work, combined with demonstrations, recitations and, when deemed necessary, lectures, in the Laboratories of Anatomy, Physiology, Physiological Chemistry, Pharmacology and Toxicology, Pathology and Bacteriology. During the last two years the student is given abundant opportunity for the personal study of cases of disease, his time being spent largely in the Hospital Wards and Dispensary and in the Clinical Laboratories. Especially advantageous for thorough clinical training are the arrangements by which the students, divided into groups, engage in practical work in the Dispensary, and throughout the fourth year serve as clinical clerks and surgical dressers in the wards of the Hospital.

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As candidates for the degree of Doctor of Medicine the school receives:

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2. Graduates of approved colleges or scientific schools who can furnish evidence: (a) That they have acquaintance with Latin and a good reading knowledge of French and German; (b) That they have such knowledge of physics, chemistry, and biology as is imparted by the regular minor courses given in these subjects in this university.

The phrase "a minor course," as here employed, means a course that requires a year for its completion. In physics, four class-room exercises and three hours a week in the laboratory are required; in chemistry and biology, four class-room exercises and five hours a week in the laboratory in each subject.

3. Those who give evidence by examination that they possess the general education implied by a degree in arts or in science from an approved college or scientific school, and the knowledge of French, German, Latin, physics, chemistry, and biology above indicated.

Applicants for admission will receive blanks to be filled out relating to their previous courses of study. They are required to furnish certificates from officers of the college or scientific schools where they have studied, as to the courses pursued in physics, chemistry and biology. If such certificates are satisfactory, no examination in these subjects will be required from those who possess a degree in arts or science from an approved college or scientific school.

Candidates who have not received a degree in arts or in science from an approved college or scientific school will be required (1) to pass, at the beginning of the session in October, the matriculation examination for admission to the collegiate department of the Johns Hopkins University, (2) then to pass examinations equivalent to those taken by students completing the Chemical-Biological course which leads to the A. B. degree in this University, and (3) to furnish satisfactory certificates that they have had the requisite laboratory training as specified above. It is expected that only in very rare instances will applicants who do not possess a degree in arts or science be able to meet these requirements for admission.

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SPECIAL COURSES FOR GRADUATES IN MEDICINE.

Since the opening of the Johns Hopkins Hospital in 1889, courses of instruction have been offered to graduates in medicine. The attendance upon these courses has steadily increased with each succeeding year and indicates gratifying appreciation of the special advantages here afforded. With the completed organization of the Medical School, it was found necessary to give the courses intended especially for physicians at a later period of the academic year than that hitherto selected. It is, however, believed that the period now chosen for this purpose is more convenient for the majority of those desiring to take the courses than the former one. The special courses of instruction for graduates in medicine are now given annually during the months of May and June. During April there is a preliminary course in Normal Histology. These courses are in Pathology, Bacteriology, Clinical Microscopy, General Medicine, Surgery, Gynecology, Dermatology, Diseases of Children, Diseases of the Nervous System, Genito-Urinary Diseases, Laryngology and Rhinology, and Ophthalmology and Otology. The instruction is intended to meet the requirements of practitioners of medicine, and is almost wholly of a practical character. It includes laboratory courses, demonstrations, bedside teaching, and clinical instruction in the wards, dispensary, amphitheatre, and operating-rooms of the Hospital. These courses are open to those who have taken a medical degree and who give evidence satisfactory to the several instructors that they are prepared to profit by the opportunities here offered. The number of students who can be accommodated in some of the practical courses is necessarily limited. For these the places are assigned according to the date of application.

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ON THE STUDY OF ANATOMY.¹

By LEWELLYS F. BARKER, M. B., *Tor.*

Professor of Anatomy, University of Chicago.

With the advent of October, with its cool and bracing days and restful nights, there is regularly a quickening of activities in academic circles. The occupant of a professional chair, reinvigorated by temporary sojourn in forest or field, at the seaside or in the hills, resumes his teaching with renewed enthusiasm, and engages again in that original investigation which represents the most absorbing interest of his life. The

student, too, perhaps, as yet less conscious of the actual need of an occasional remittance from his labors, has nevertheless had his holiday, and returns to the college of his choice ready for another season of diligent application and eager to begin once more the arduous tasks which the pursuit of knowledge entails.

It has long been customary in colleges in which medicine is taught to call a meeting of the faculty and students at the beginning of the autumn session. Such a meeting permits of the reunion of former teachers and students and the intro-

¹ An address delivered before the Faculty and students of Rush Medical College, October 5, 1900.

duction and welcoming of new teachers and new students. It gives, further, opportunity for the making of certain special remarks; and I have noticed that there is almost universally a tendency on the part of the faculty to grant the privilege of remark-making to some member of it who has lately been added to the staff. Being myself one of the most recent additions to an already large staff-family, the privilege has this year been gracefully allotted to me. However great a sacrifice on the part of my colleagues this may represent, I can assure you that the new-comer on this occasion, like the distinguished member of the faculty who last year addressed you, considers it a great favor to have the opportunity of expressing the pleasure he has in coming among you and being counted one of you, and to meet with an occasion on which he can more or less generally indicate the aims and scope of the science which he represents, and so publicly justify the position which he holds. Fortunately, in this latter respect the task is an easy one, for anatomy has in medicine long ago won its place as a science essential as a basis for all the subsequent medical studies, and moreover, my predecessors in office have been men of such sterling merit, power and inspiration, that the subject is here appreciated and revered. Especially true is this of him who has immediately preceded me as the occupant of the chair, and who has left it in order to accept a chair in surgery; while we commiserate anatomy on losing so able a representative, we must congratulate surgery on the enlistment in its service of so well trained and enthusiastic an anatomist. He has at this college developed, among other things, a course in surgical anatomy—easily one of the best given in America—and this part of the anatomical work, I am glad to assure you, he has promised, for the present at least, to retain. You join with me I know in wishing my colleague, Professor Bevan, a continuation of that success which he has already attained in the field of his ultimate choice.

The year in which we live marks an important epoch in the history of the college. Of a whole series of advances, I wish to call attention especially to one. Beginning with this autumn quarter, a closer relationship than has ever before existed between Rush Medical College and the University of Chicago has been established. Not entirely satisfied—for what true lover long is?—with that “sisterly” relationship which the term “affiliation” represents, the college has this year appointed to two of its fundamental chairs—physiology and anatomy—men who are already the occupants of chairs in the same sciences at the university. That such closer bond of union cannot fail to be of the greatest value, both for Rush Medical College and for the University of Chicago, I confidently believe. That it is only the forerunner of a still deeper intimacy, many, I am sure, both in the university and the college, fondly hope.

On thinking over anatomical subjects in the search for material for this address, the ideas which came to me grouped themselves in the main under two headings: (1) What does the science of anatomy include? and (2) How can the study of anatomy best be prosecuted? Each of these headings cor-

responds to matter enough for a single occasion; I have, therefore, decided to spend the time at my disposal this evening in a consideration of the former of the two questions, and to reserve for another time and place what I have gathered in answer to the latter.

Of the whole group of the natural sciences, there is perhaps no other member, the province of which is less well understood by the general public than is the science of anatomy. As ordinarily thought of by the layman, it is a science the study of which necessarily precedes the practical work of medicine and surgery; a science which is largely, if not wholly, descriptive, and one which to be mastered requires prolonged occupation, scalpel in hand and pipe in mouth, with dead and partially decomposed human beings. Such a view of the science, though perhaps not surprising when we recall the methods by which anatomy—so-called—has frequently in this and other countries been prosecuted, could, I do not need to tell you, be scarcely more widely removed from the truth. Anatomy is not simply a descriptive science; the study of it as a preparation for practical medicine and surgery represents only one side of its interest and usefulness; the scalpel is now perhaps the coarsest instrument it employs; its work is by no means confined to the human body alone, much less to the dead human body, and when it does deal with the latter, the material can be so well preserved that even the fragrant Havana is said to be more offensive to some sensitive souls than are the odors from the well kept preparation room.

Even medical men differ markedly in their conception of what anatomy includes, their ideas being based largely upon the kind of anatomy they themselves were taught, and upon the anatomical needs of the particular branch of medicine which, after graduation, they have cultivated.

Nor is there uniformity of opinion among the pure anatomists themselves, as can be readily seen by a perusal of the various addresses made by scientific anatomists in different parts of the world during the last twenty years. A free expression of opinion upon the subject has, however, gone far to make the aims and scope of the science clearer, until at present its principal representatives are more nearly in accord with regard to them than ever before.

In what this accordance consists, I can, I believe, make clearest to you by glancing briefly at the various steps through which the science has passed from the period when the earliest anatomical observations were recorded to the present day.²

² In the preparation of this address I have made free use of a large number of addresses made on similar occasions by other anatomists. I have had no hesitation in borrowing liberally as will be immediately apparent to those who are familiar with the bibliography. Especially useful to me have been the addresses and papers of His, Hertwig, von Kölliker, Macalister, Mall and Waldeyer. The following are some of the sources consulted:

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There can be no doubt that from the earliest times, curiosity concerning and interest in the make-up of the human body has existed. The references to man's body and its organization frequently to be met with in the pages of the old Hindu Vedas and of the earliest writings of all the Oriental nations make this evident. Nevertheless, the awe in which men stood before the human cadaver, together with the penalties threatened by religious leaders for its molestation appear to have effectually prevented any systematic examinations and the little knowledge possessed by the ancients, aside from the conclusions drawn from animals killed for food or for sacrifice, seems to have been drawn from the instances in which, through the violence of war, the chase, or of the natural elements, the human body became dismembered or eviscerated.

The earliest dissections of the human body of which no doubt exists are those which were undertaken at the Alexandrian School (B. C.) by Herophilus and Erasistratus, supported and protected by the intelligent Ptolemaic rulers. The name of Herophilus is still familiar to every beginner of anatomical studies in the term *Toreular Herophili*. The statement is made, though I hope it is not true, that these daring anatomists went so far, with Ptolemy's sanction, as

to dissect living criminals, from which Tertullian designated Herophilus as *lanius* (Fleiseher).

This opportunity for the anatomical investigation of the human body appears to have been unique, and it continued only for a short time. Even Galen's studies, the results of which were held for the following ten centuries at least to be infallible, were limited to the bodies of animals; he recommended, it may be remembered, the study of the bodies of apes and swine—the animals which in his opinion were nearest to human beings. After Galen, the natural horror which the examination of the dead body excites, together with the edicts of the church against dissection, prevented any further progress of descriptive human anatomy for a very long period. The church declared that Galen had been infallible, and that therefore no further anatomical studies were necessary. Fortunately for science, which knows but little infallibility, certain of its votaries in high favor at Rome gained permission, in the fourteenth century, to make dissections of human bodies, and to use them for demonstration before students. Mondini in Bologna again opened the path for scientific anatomical inquiry and started in Italy a movement which placed that country, as far as medicine is concerned, in the lead. Students from distant lands were at-

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tracted, as they always have been and always will be, to the point where progress was making the greatest headway.

The great Vesalius, often known as the father of anatomy, was among these wandering scientists. Born in Belgium and educated in France, he prosecuted his anatomical studies in Italy, especially when professor at Padua, to such a degree that he merits a place among the world's greatest reformers. This energetic, truth-seeking, idol-breaking, authority-denying man, dared to look at things as he saw them rather than as Galen had said that they should be, and thus made discoveries of the first importance in anatomy; by his artistic powers he rendered many of them imperishable; best of all, he broke forever the tyranny of tradition in anatomical knowledge, and threw wide open the gate by which men must always enter in the pursuit of anatomical truth. Vesalius was a contemporary of Luther; the year of his death is that of the birth of Galileo and of Shakespeare.

It was the spirit which animated Vesalius which later led William Harvey, the founder of physiology, to the discovery of the circulation of the blood, and Giovanni Battista Morgagni, the founder of pathology, to that mode of conception which Virchow has designated "the anatomical idea in medicine." It is the spirit which is embodied in every scientific worker of to-day who accepts the records of past investigation only as a guide—a guide which must be fallible since it is human—and which, therefore, must be repeatedly controlled; a guide which needs constant revision on account of the ever-increasing extension of the domain of sense, and one, which, if not added to significantly by the scientist in his lifetime, will stand as an everlasting witness to his inefficiency, a perpetual testimony to his lack of consequence.

Like all the natural sciences, anatomy in its earlier stages consists, of necessity, in the amassing in an empirical way of a store of naked facts. In other words, the subject is purely *descriptive* until a sufficient number of facts have been collected to make their arrangement and classification a task worth while. Adequate descriptions are based upon intelligent *observation*, which in turn is dependent upon the skillful use of the organs of sense, including the means which modern technique is ever inventing to extend them. The body is examined externally and internally in its various parts; it is looked at; it is felt. The size, shape, color, weight, consistence and reciprocal relations of the parts are noted; the results are recorded, the attempt being made to establish the material content of the science with all possible certainty, sharpness and clearness. The parts have first to be distinguished and named; then accurately described, their physical characters being established in language. The description of a natural object that shall call up in the mind of the reader a precise image of the object and that shall serve as a reliable guide to a succeeding observer, does not fall within the province of every man's capacity; happy indeed is the anatomist who possesses the power, for as has more than once been pointed out, an exact and clear description of the known is often of as great value as the so-called "discovery" in the region of the unknown.

The satisfactory naming of the various parts alone is a task of far greater difficulty than at first appears. An object must be studied for a long time, in many countries, and by men who know the relations of anatomy to every subject with which that science is allied, before a name for a part which shall be in accord with all the requirements can be decided upon. Almost every part has at various times received a series of names; periodical revisions of nomenclature by representative committees are accordingly desirable in order to arrive at uniformity among anatomists and to relieve the science of an immense number of names, since at best it must be grievously burdened.

Ever since the time of Vesalius there has been an unbroken series of anatomical observers who have devoted their powers to the attaining of skill in dissection and anatomical description. With energy and endurance and often at great personal sacrifice, this band of anatomists has developed this side of our science until it has reached the degree of precision which characterizes it to-day; a state indeed which many believe to be practically complete and incapable of further progress. Of the difficulties overcome by Americans in helping with this work since Mr. Giles Firman made the "first anatomy of the country," a good idea can be gained from the admirable historical review which we owe to E. M. Hartwell. While it is obvious that there must be a temporal limit to the discoveries which the naked eye is to make in anatomical fields, one has nevertheless only to refer to the current journals to see that the limit has not yet been reached. But the limits of progress in anatomical description will by no means be synchronous with those of macroscopic discovery of the objects themselves, indeed, considering the complexity of man's architecture and the different and ever-varying view-points whence descriptions are being written, it is scarcely conceivable that man will ever attain to descriptions which will be satisfactorily final. To the surgeon, to the artist, to the physiologist, to the scientific anatomist, the details of parts are of utterly different significance; the varying scale of anatomical values requires in each case a special description; an objective characterization of all details, merely as such, would make anatomical descriptions so ponderous and chaotic as to render them totally useless to any one. Nor can anatomical illustrations, in colors and otherwise, which are perhaps even more valuable than anatomical descriptions, ever be completely objective. The exact plates of anatomical objects which approach of late years ever nearer to that degree of accuracy which will permit of the taking from them of mathematical measurements, never attain actually to perfection; there must always be an element of subjectivity in them which may be inconsonant with the needs of some other observer at some other time.

Again, the greater or less degree of variability to which all parts of the animal body are subject, makes it difficult for anatomists to agree as to what shall be called normal, and thus the same object has frequently to be described in several different ways and multiply and exactly represented in pictures. There thus remains and ever will remain a task for

the anatomist in the domain of anatomical description and of anatomical illustration.

If it be true that in the fields just referred to there is still much work to be done, the statement is all the more justified with regard to the taking of measurements and weights of the body and its parts. The shape of the natural objects is nearly always such that the localization of fixed points whence measurements can be taken is rendered very difficult—so difficult that frequently the comparison of the measurements of one observer of an object with those of another observer of the same are useless. Again, owing to the variability of the bodily dimensions in the two sexes, in different races, at the various ages of life, according to individuality or under different physiological conditions, unless a whole series of data accompany a given measurement, the result may be of no value to a succeeding observer. In modern anthropology, however, definite criteria are always attended to and the measuring method is proving to be of the highest service in the elucidation of the questions that science has to solve.

The difficulties of anatomical measurement in large part obtain also when the weighing of anatomical objects is undertaken. Notable results have already been obtained, however, not the least of those in connection with the central nervous system being gained through the comparatively recent work of my colleague, Dr. Donaldson, in the university. The application of the method to the determination of the normal by Thoma may also be referred to as the beginning of a long series of investigations which, in the end can scarcely fail to be of the greatest importance. As His, who has discussed this and the foregoing subjects in an admirable manner, points out, it is difficult to imagine how the study of variations in constitution is to be approached unless this and similar methods are employed. As he says, it must be of decisive influence for the physiological capability of an individual, whether in his organization the musculature predominates over his nervous system, his epithelial tissues or his glandular organs, whether his heart is relatively large or small, whether accordingly it can increase the average blood pressure in the arteries to a great or to a slight degree, whether the man has a large or a small liver or whether he has a long or short alimentary canal. The study of anatomy with the unaided sense-organs is, as we have seen, one of no small magnitude, and one not yet completed. What then is to be said of that descriptive anatomy which invades the territory in which the eye only with the aid of the microscope can penetrate? The field of the microscopical anatomist is at least a thousand times wider than that of the macroscopic worker, and in that field, what has been said above concerning description, pictorial representation and anatomical measurement, equally holds good. It will yet be long ere the collection of microscopical data will have been completed. New methods open up new problems, and at present progress, descriptive and microscopical anatomy may probably occupy workers for centuries to come. Even with the methods and microscopes now at our disposal, we have entered a museum, the largest part of which has yet to be accurately catalogued,

and who can say what new doors the methods and the microscopes of the century just before us are about to open up? The science of histography is almost as undeveloped as was geography before the voyage of Columbus. Between the histographic world of to-day and the architectural world of stereochemistry who will dare to prophesy what rich territories may exist?

The mere observation and registration of naked facts does not, however, satisfy for long the cravings of the investigating human intelligence. Indeed, there is something of a blunting character about the process if long continued without the synchronous operation of other faculties of the intellect. Man is a *classifying* and *generalizing* animal; there lies deep in his nature a desire to *arrange* the facts he observes in an orderly manner, with the object of *understanding* them. It is in the attempt to satisfy this human tendency that anatomy, instead of remaining a purely descriptive science, becomes elevated to a plane on a level with the other inductive sciences.

Evidences of attempts at anatomical classification are found among the earliest anatomists. The close resemblance of certain parts of one another soon gave rise to the idea of organic systems; such as the muscular system and the nervous system. The keen observations of Aristotle on the *partes similes* and the *partes dissimiles* may be recalled, as well as those of Fallopius outlined in his *Tractatus quinque de partibus similaribus*. It was left to the organizing brain of the young Frenchman, F. Xavier Bichat, to get a grasp for the first time of the relations of elementary *tissues* to the general architecture of the body. Although, through overwork and impecuniosity, his penetrating eyes were forever closed at the early age of about 30 years, Bichat left behind him three treatises—his “*Traité des Membranes*,” his “*Recherches physiologiques sur la vie et la mort*,” and his “*Anatomie générale*”—a legacy so immense that we cannot help lamenting with wondering regret the too early arrest of his labors. He recognized the fact that whereas in chemistry the more complex bodies are composed of simple elements, so in the architecture of man's body, simple *tissues* are variously combined to form the complex mixture of tissues which are ordinarily known as organs. He distinguished some 21 *systems* or *tissues*—the cellular, the osseous, the fibrous, the cartilaginous, the nervous, the muscular, the medullary, etc., basing his classification on the manner in which each tissue behaves in the presence of various reagents, the physical and vital properties of each and, finally, the character of each when met with under diseased conditions. In other words, Bichat was the founder of the modern science of *histology*, or, as it is sometimes designated, “*General Anatomy*.”³

Before following the progress of anatomy further along this line, a word must be said concerning what must be regarded perhaps as the first direction taken by the investigat-

³ Cf. Duval, M.: *L'Anatomie générale et son histoire*. Rev. Scient. Paris, 1886, xxxvii, 65, 107.

ing mind toward the *understanding* of organic forms—namely, the physiological (in its first stages, the purely teleological).

As has long since been pointed out, the language of anatomy is sufficient evidence of the long existence of the teleological conception in this science. For thousands of years the individual parts of the body have been known as “organs,” and the processes going on in them as “functions.” Just as function was unthinkable without a corresponding organ, so an organ without function was inconceivable, and thus wherever, in the series of well-understood parts of the body, one remains over whose purposeful participation in the processes of life is not understood, towards this is directed over and over again the mental acumen of the investigator to assign to the reluctant organ a definite significance.⁴ It is not my purpose here to enter into a discussion of teleology. The world has been widely enough explored to utterly dispose of that gross anthropomorphic form of teleology which pointed to a humanly scheming architect of the universe, and whether or not we accept some more correct form of teleology is, at present, matter for individual opinion. This much is certain, that while no teleological view of nature actually *explains* the organization of a human body, the teleological conception has been particularly heuristic in its effects in the investigation of the relation between the physical processes in, and the physical characters of, the various parts of the body. Ever since Galen, though animated by a false teleology, wrote his *De usu partium*, in which the size, position, number, consistence and structure of the various parts are treated as facts which can be understood only through the investigation of the purposes which they subserve, this mode of consideration has been among the most influential. Even to-day a large part of the profitable research undertaken by anatomists, physiologists and pathologists, has for its aim the elucidation of the relation of structure to function, especially in microscopic domains. The work done in Ludwig's laboratory was largely of this nature, and as recently as 1883, H. v. Meyer⁵ has asserted that the only possible way of understanding the organs is to proceed to the study of them from the physiological view-point. But if this were true, then all scientific anatomy would be physiology, a statement which narrow-minded physiologists might applaud, but which broader men know to be untrue. Physiology is one of the daughters of anatomy, and is not likely so soon to forget the fifth commandment. Johannes Müller was the last great scientist who covered both fields of anatomy and physiology; since his time investigators have cultivated one of the two at the expense of the other, a division of labor which we must recognize on the whole as beneficial, though that it is accompanied by certain drawbacks must also be confessed. Especially difficult is it to sharply separate the study of structure from that of function in the science of cytology, founded by Schleiden and Schwann, pupils of Johannes Müller in the

fourth decade of this century. The development of the cell-doctrine, modified as it was somewhat later by the introduction of the protoplasm-theory by Max Schultze, marks a most important epoch in the history of both anatomy and physiology. Its value for the more practical side of medicine is sufficiently in evidence when one of its direct outgrowths, the cellular pathology of Rudolph Virchow, is recalled. The appalling elaboration of technical methods during the last few years has led to the accumulation of cytographic data which remove all the comfort we once had in looking upon the cells as elementary structures. Though cytophysiology is as yet far behind cytography in its state of development, there no longer remains any doubt that in approaching the cell we stand before an organism of enormous complexity of constitution, endowed with functional activities which must for long remain to us unfathomable. Any one who has worked much with protoplasm and nucleus, with archiplasm and centrosome, with cell-fibrils and cell-granules under various physiological conditions, cannot fail to appreciate the fact that here only the threshold of inquiry has been crossed—the exploration of the real nature of the cell only just begun. Indeed the evidence is fast accumulating in favor of the opinion that many of these morphonuclear cell constituents represent precipitates due to the action of reagents, and the laws governing their regular appearance under definite conditions are being investigated. It is exactly in these studies that structural and functional investigation still do well to go hand in hand, a fact which a survey of the cytological handbooks, now becoming so numerous, will show, is meeting with general recognition. I believe it was Du Bois Reymond who ventured the statement that “an ocean steamer with all its machinery and intricacies of construction is far less complicated in its composition than a cell.” Would that the cell were no more complicated than the ocean steamer in construction!—the modern investigator would then soon be ready with the solution of its problems. Alas! the difficulties are not confined to the study of these organisms as individuals; already we have entered upon the investigation of their social relations, and cell-altruism and cell-egoism, cell-states and revolutionary cells are discussed as actively among cytologists as are the similar social questions concerning organic individuals of another order by the people at large. Further, in cytophysics and cytochemistry, research is at present most active—these subjects representing one of the most interesting subdivisions of recent physiology. Should the gulf between the present microscopic picture of the cell and its chemical structure ever be bridged, stereochemistry would enter into the domain of anatomy. So much in general, with regard to the physiological view-point in anatomy.

Closely allied to the foregoing, and in reality an offshoot from it, is the mode of consideration of the surgical and topographical anatomist. In this branch, the individual regions and cavities of the body are dealt with with regard to the reciprocal position of the various organs and systems. Surgical anatomy studies these relations only in so far as they are of importance in operative procedures; topographical an-

⁴ Cf. His, W.: Ueber die Bedeutung der Entwicklungsgeschichte für die Auffassung der Organische. Natur. Leipzig, 1870.

⁵ v. Meyer, H.: Stellung und Aufgabe der Anatomie in der Gegenwart. Biol. Centralbl., 1883, No. 12.

atomy, a wider subject, studies the relations mentioned and independently of their significance to the surgeon. The various regions of the body are studied sometimes in layers, sometimes with regard to serial clues to a particular structure. Sections of frozen cadavers have here proved to be of great value for the study of relations and for helping the student to make mental reconstructions of the parts analyzed by dissection. Surgical and topographical anatomy are thus seen to be subjects of very high practical importance—the former especially for the surgeon, the latter also for the worker in internal medicine. It is this kind of anatomy which has been brought to so high a state of cultivation in Great Britain, and especially in London, where most of the anatomy has been taught by men in surgical practice. Valuable as such instruction is for surgery and medicine, it should not be forgotten that it is applied anatomy rather than anatomy proper, and no less a scientist than Macalister has deplored the lack of advances in anatomy in England, attributing it largely to the one-sided mode of instruction in vogue, and to the examinations, to the passing of which the teaching is in large part directed. Surely certain morphological considerations are as important for the student of anatomy as the learning by heart of the various relations of an artery, especially if the student is not to become a surgeon; it would be melancholy indeed if there were not at least some members of the anatomical classes who regard the study of the architecture of the brain and spinal cord as interesting and as important as that of the perineum.

But anatomy as a science would never have attained to the dignified position it now holds had the minds engaged with it remained satisfied, after observing and registering its material content, with attempting the explanation of the human body from the physiological view-point or by exhausting the possibilities of its relation to the surgeon's knife.

As in the other natural sciences, the causality-need of the intelligence has forced the anatomist to undertake the investigation of the *origin* of the organic forms which he studies, and of the relations of these forms to other similar and dissimilar organic forms accessible to examination. In other words, the comparative and the genetic methods of study have been resorted to. Comparative anatomy and embryology together constitute morphology, at least in the sense in which the term is ordinarily used, and in morphology we recognize the part of anatomy which makes it truly worthy of being designated a science.

In the application of the comparative method, not only are the different parts of the human body compared with one another—the arms with the legs, the brain with the spinal cord, the skull with the vertebral column, the various segments and segmental partitions with one another—but man, recognized as a member of a long series of *animals*, is compared with each of them in turn, and they with one another, with the object of establishing groups of type forms and of learning the plan of architecture, not only of the single creature, but also of the whole series. At first, anatomists studied the forms which to them seemed to resemble man most closely, but the

gradual transition from one form to another was so striking that animal after animal was studied until finally the whole world of organisms has been submitted to the examination of the comparative investigator. Oken and Goethe, Cuvier, Meekel, Geoffroy, St. Hilaire, Lamarck, Wallace, Darwin, Haeckel, Huxley, Gegenbaur and Leidy are names which have become very familiar to us in this field. The world of living creatures is a unitary system, of which man is an inseparable portion. First, when the whole system has been worked through do the form and significance of many of man's parts become intelligible. The animal series can be thought of as a tree with the simplest forms at the root, the trunk branching at its origin, each branch in turn subdividing into limbs and twigs until the highest degree of differentiation is reached. It is this recognition of the lawful relation of organisms to one another which the study of comparative anatomy has afforded us. Such a recognition, now general, was little less than startling to those who first arrived at it. That it pointed to some more general law was obvious. As Goethe himself, no mean participator in comparative studies, beautifully expressed it:

“Alle Gestalten sind ähnlich und Keine gleicht der andern,
Und so deutet das ehor auf ein geheimes Gesetz.”

Has this secret law been discovered? Many believe so and look upon Darwin's doctrine of descent as a generalization worthy, on account of its scientific value, of being placed side by side with Newton's theory of gravitation. Whether the evolutionary doctrine be unequivocally accepted or not, certain it is that the relationship of forms which comparative anatomy reveals, finds in this genealogical conception of Darwin a more satisfactory explanation than any other hitherto offered.

Closely allied to the phylogenetic mode of consideration is that which we designate as the embryological ontogenetic or developmental. In the human species, as in every other, the life of the individual member is of short duration; each human organism has a beginning, a period of growth and development, followed, even in the life of maximum length, in the course of a few decades, by decline and death. Generation follows generation as wave follows wave on the surface of a ruffled sea. In the transference of life from one generation to another the material substratum sinks to a minimal amount—the new human being begins as a fertilized egg-cell 1-120 of an inch in diameter, weighing only a minute fraction of a gramme. From this simplest of beginnings it gradually passes through a long series of developmental stages, the character of these stages varying somewhat under environmental influences, each stage being the unnecessary consequent of a preceding stage, and at the same time the necessary antecedent of the stage which follows it until finally the organism attains to the fullness of differentiation of which, under the circumstances of its environment, it is capable.

In this long series of developmental stages which every mammal passes through, the earliest are very, very simple and correspond in form closely with the lower forms in the animal kingdom. But as cell-division in the embryo proceeds, the

shaping of the organism becomes more complex, resembling higher and higher forms of animal life, until finally that of mammals is assumed. Even at this period the unskilled observer might easily be confused if he were required at a glance to distinguish a human embryo from those of several other mammals at a similar period of development. Ultimately, the differential characters of the species become clearly marked, and even the tyro can easily recognize them. The more skilled the observer, however, the earlier in the development will the species-criteria be decisive.

Comparative embryology becomes all the more astonishing a study when we realize that the embryological history of every higher animal is, for a long period at least, almost identical with that of a whole series of allied forms. No wonder, then, this state of things being acknowledged, that the embryologists, like the comparative anatomists, have pictured the genetic relations of the different animal forms also as a tree, a tree which on close examination is found to accord very closely with the tree of relationship constructed by the comparative anatomists.

Comparative anatomy and embryology are, therefore, closely interwoven subjects, and each may, in a way, be looked upon as a control for the other, though each has its special problems, and each sets about the solution of these in a manner peculiar to itself. Take, for example, the attempts at an explanation of the series of forms through which the individual passes in its development. Many comparative anatomists, accepting Darwin's doctrine of the origin of species through a struggle for existence among generations influenced by heredity and variation, would explain the development of the individual member of a species as a temporarily compressed recapitulation of the developmental course of the species as a whole. While this doctrine that "ontogeny repeats phylogeny" has been maintained by eminent scientists there are others who are unwilling to accept what cannot be proved; and some of the embryologists especially feel it their province to attempt to explain from embryological studies alone, and without reference to phylogenetic history, the origin of the various form-stages through which the individual passes. Already great strides have been made in the direction mentioned, especially through the investigation of the laws of growth; and the field of developmental mechanics, though so lately entered upon, has proven to be one of the most fruitful of those thus far tilled. One of the foremost investigators along these lines goes so far as to assert that the growth of every organic germ must, as a process strictly regulated according to time and space, possess a mathematical expression in which the velocity of growth of each point is determined in its dependence on the time and the position. Whether such formulæ will ever be set up and the kingdom of organic forms thus subordinated to the domination of simple numbers, seems doubtful, but in any case the conception is an interesting one. We need not, however, look into the nebulous distance for the advantages to accrue from developmental study. Near at hand are thousands of facts of the greatest importance for anatomy as a whole and for

the practical branches of medicine and surgery to be gained only through this method of study. Scarcely a part of the body but what is now better understood than was otherwise possible. I need only mention the remarkably complicated morphology of the brain and the sense organs, the distribution of the intestines, the grouping of the various voluntary muscles, the puzzling course followed by certain of the nerves and of the reproductive organs in the two sexes, to call to mind some of the features which embryology has gone far to illuminate.

I dare not pass by unnoticed here two phases of investigation which naturally follow upon the others, but which have only very recently begun to be extensively cultivated, viz.: those of histogenesis and of comparative histology. Histogenesis stands in the same relation to comparative histology as does embryology to comparative anatomy. Indeed, it is simply pushing the microscope into embryology and comparative anatomy, and is, in a way, comparable to the advance from gross descriptive anatomy to microscopic anatomy. By histogenesis we mean the study of the development of the individual tissues, including that of the individual cells (cytogenesis). By comparative histology and cytology we refer to the comparative microscopic study of the various tissues and cells through a series of animals. The light thrown upon many of the unsolved problems of structure by these methods is unexpectedly brilliant, and the future has much to hope from it; MacCallum, too, has shown how important these methods can be in helping to explain certain pathological phenomena met with in heart-muscle, and there can be little doubt that we are on the brink of the discovery of a series of relations between histogenetic conditions and pathological processes.

Lastly, as a crowning piece to the whole system of anatomical study, experimental morphology must be recognized. As but a child among the kindred sciences, it is of robust constitution, being the offspring of vigorous parents, and, in this country especially, in an environment most suitable for its healthy growth. The anatomist is no longer confined to the study of adult forms, or of forms in their natural mode of development; he can now, to a certain extent, artificially control form-production by resorting to the experimental method. The experiments which have been made upon heteromorphism, upon the artificial production of malformations, and upon the grafting of embryos, are full of interest, so much so as to disturb the equanimity of the soberest of scientists. During the last year or two we have been—I was going to say—shocked by the bringing of the proof by my colleague, Professor Loeb, that the eggs of several forms not naturally parthenogenetic can be fertilized—or at any rate, brought to development in the absence of spermatozoa, solely through the action of (?) physico-chemical influences. With miracles such as these already performed, we can but stand in awe of the work of the future.

Most sketchily and imperfectly I have tried to give you an idea of what the study of anatomy includes, viz.: descriptive or systematic anatomy (gross and microscopic), physiological

anatomy, surgical and topographical anatomy, histology or general anatomy, including histography and cytology, comparative anatomy, embryology, comparative histology and embryology, histogenesis and lastly experimental morphology. Assuredly the subject is wide. It is, I am sorry to say, too wide to be mastered in all its details even when a whole lifetime is devoted exclusively to it. The scientific anatomist, after familiarizing himself with the main facts and principles of its various subdivisions, does best, in agreement with the great law of division of labor, to direct his efforts towards the acquisition and promulgation of knowledge in some one portion of it.

And now for a word of welcome to the class just entering upon the study of medicine. You have taken, gentlemen, the first direct step which is to lead you into one of the noblest professions in the world—into a profession in which your lives are to be consecrated to the service of suffering men and women. You have to learn the laws which govern health and those which underlie disease. You, like your predecessors, will find that a large proportion of your time and energy in life will be directed toward the prevention of the occurrence of disease, rather than to the cure of it, for medical men have the proud distinction of being perhaps the only workmen “who make it their first duty to stop the sources of supply from which they derive their income.” Hard work during the next four years will be required of every one of you; indeed, your time will be so occupied and your mental powers so strenuously engaged that you will have but little opportunity for recreation or for the amenities of life. But while this is the most difficult period of your career as far as intellectual work is concerned, do not, I beg of you, forget altogether the *man* in the making of the physician or surgeon. However much your instructors may stimulate you, however much work they may ask you to do, you will be wise if you retain some period of the day, be it only half an hour or even less, when you can withdraw from men and medicine and in some quiet nook indulge a wholesome longing for good general literature. Keep your old friends by you—your Plato and Marcus Aurelius, your Emerson, Carlyle, your Dante, Shakespeare and Milton, your Goethe, Shelley and Keats. If your osteological studies prove refractory you may find the stoicism of Epictetus a remedy for your disturbed spirit; after the depressive influences of pathological anatomy the lyric of Goethe, the raptures of Shelley, or an essay of Stevenson may prove to be uplifting; to combat the intoxicating fumes of the chemical laboratory try the antidotal effects of Burton, of Sterne or of Rabelais. The time so spent will not only be revivifying for the moment, but will be of the greatest value to you in your professional life after graduation. Skill is more and more revered, but skill without culture has lost half its power. And culture, like reputation, has not only to be gained but to be kept, nor is it gained or kept without effort, without constant vigilance.

Permit me to hope that you have laid broad foundations in the sciences which are fundamental for medicine; viz.: physics, chemistry and biology. Without thorough training in these it is impossible to keep abreast of the rapidly swelling tide of discovery in modern medicine. If, further, you are familiar with the French and German languages you will find it possible to become conversant with important new facts and discoveries months and sometimes years before they enter into the English text-books. Of the distinctly medical sciences, anatomy, physiology and physiological chemistry, together with pathology, form the framework upon which all the rest of the medical sciences are built. Failure to make this framework solid renders the superstructure inevitably unsafe. Do not forget that the medicine of to-day differs from that of the years close behind us chiefly in the substitution of “handcraft” for much of the former “redcraft.” In these days, too, as it has well been put: “The eye cannot say unto the head, I have no need of thee.” Instead of accepting the statements of others about things as of yore, the medical student is nowadays being made to *do* things. Instead of memorizing text-books, quiz compends and lecture notes, he is more and more required to study the natural objects, to observe accurately, to record concisely and adequately, to experiment intelligently. While good lectures, good recitations and good text-books still have their place, the student is wisely encouraged to interrogate Nature for himself and to believe in the replies he obtains from her rather than to put implicit confidence in the descriptions of others.

The new methods of medical education are costly; they demand large laboratories, expensive equipment and scientifically trained instructors. They cannot be satisfactorily introduced into schools where the sole income is derived from the fees of students; large endowments are absolutely essential for the proper carrying out of the plan.

Finally, gentlemen, let me give expression to the hope that among this class now entering, besides the large number who will go on into beneficent and successful practice, there may be some who, willing to scorn delights, to live laborious days, will set before them the high hope of making actual additions to knowledge. It is not fair that we should accept the gifts of our forerunners without making the effort ourselves to enrich the general stock of knowledge. The paths of investigation are not smooth; the way of research is difficult. But the goal is strife-worthy, and the rewards are sufficient.

In closing then let me quote those stirring words of the sage of Chelsea, which I excerpt from his *Sartor Resartus*.

“Produce! Produce! Were it but the pitifulest infinitesimal fraction of a Product, produce it in God’s name! ’Tis the utmost thou hast in thee: out with it then. Up, up! Whatsoever thy hand findeth to do, do it with thy whole might. Work while it is called To-day, for the night cometh, wherein no man can work!”

ON THE OCCURRENCE OF TAILS IN MAN, WITH A DESCRIPTION OF THE CASE REPORTED BY DR. WATSON.

BY ROSS GRANVILLE HARRISON, PH. D., M. D.,
Associate Professor of Anatomy, Johns Hopkins University.

Some years ago Bartels¹ gave an excellent *resumé* of our knowledge and beliefs concerning the occurrence of caudal appendages in man, showing that references to this peculiarity are to be found as far back as the writings of Pliny and Pausanias. Appended to Bartels' paper is a map, which shows the various lands supposed at one time or other to have been the haunts of human races with tails. These regions include not only widely distant portions of South America, Asia and Africa, but also the greater part of western Europe. While many of the statements cited by Bartels are to be classed as legendary, it is of interest to note how persistent and wide in range the belief in the existence of such races has been. The most remarkable stories have been told and have found credence; in these the significance of the caudal appendages has been variously interpreted. On the one hand, a tail has been considered a distinction of the highest degree, even a mark of divine descent, as in the case of the Ranas of Poorbunder;² on the other hand, it has usually been looked upon as a curse or a stigma of degradation.³

While careful investigation of the many travellers' stories has invariably given negative results regarding the existence of tailed races, so many individual instances of *homo caudatus* have been observed, that the popular belief in them has been kept alive without difficulty. With the growing interest shown by anatomists and anthropologists in the subject, the number of cases which have been reported has become considerable, and the fact that the human embryo at a certain period of development is provided with a tail-like appendage has lent color to the discussion of the question. Bartels in 1884 referred to one hundred and sixteen persons who had recorded observations upon tailed men. Of these, over sixty cases had been more or less completely described. In 1892 Schaeffer⁴ collected additional cases, adding in all twenty-five. Pyat-

nitski⁵ has also given an elaborate account of the subject, and still more recently Kohlbrugge,⁶ in connection with an admirable description of a very interesting case, has made valuable comparisons with previous work. From the United States five cases have, to my knowledge, been reported.⁷

Undoubtedly we have in these so-called tails a most heterogeneous collection of anomalies. Anything appended to the sacral or coccygeal region is described as a tail. Many do actually bear certain resemblances to the tails of lower animals, and have in fact been compared with a great variety of these. On the other hand, some are vesicular or of irregular shape and accompany the condition of *spina bifida*, while others are to be classed as teratomata or other tumors. A further very significant fact is that a large proportion of the cases have been complicated by the coexistence of *ectopia viscerum*, *hypospadia*, *atresia ani*, or deformities of the limbs, all of which are known to result from amniotic adhesions. This circumstance has led Schaeffer to the conclusion that human caudal appendages are always due to this cause.⁸

There are, however, a great many cases in which the anatomical relations of the tail are such as to indicate that it owes its existence to the persistence of at least part of the vestigial tail found in the human embryo. In some of these it seems that the coccyx extends down into the tail, though there is no good evidence that there is ever an increase over the normal number of coccygeal vertebræ in these instances. Under this latter head would come the majority of the adherent (*angewachsene*) tails described by Bartels,⁹ and also some

¹ M. Bartels: Die geschwänzten Menschen. Archiv f. Anthropol., Bd. xv, 1884.

² These were the rulers of the Jaitwa or Camari, one of the Rajpoot tribes. "They trace their descent from the monkey-god Hanuman, and confirm it by alleging the elongation of the spine of their princes, who bear the epithet 'Pooneheria, or the long-tailed Ranas of Saurashtra.'"—James Tod: Annals and Antiquities of Rajast'han, or the Central and Western Rajpoot States of India, vol. i, London 1829.

³ Bartels cites an instance of this in the stories regarding a certain community of tailed men in Turkestan. These were held in the utmost contempt by the other people, and were therefore condemned to constant inbreeding. They were referred to as "Kuju rukly Tatar," which in German is rendered "*Stinkendes Ungeziefer mit Schwänzen*." The tail was supposed to be a special curse in that it hindered the possessor from sitting properly on his horse.

⁴ Oskar Schaeffer: Beitrag zur Aetiologie der Schwanzbildungen beim Menschen. Archiv f. Anthropol., Bd. xx, 1892.

⁵ I. S. Pyatnitski: On the Question of the Formation of a Tail in Man, and of Human Tails in General, according to Data from Literature and Personal Researches. Dissertation. St. Petersburg, 1893 (Russian).

⁶ J. H. F. Kohlbrugge: Schwanzbildung und Steissdrüse des Menschen und das Gesetz der Ruchseklagsvererbung. Natuurkundig Tijdschrift voor Nederlandsch-Indië, Deel lvii, 1898.

⁷ Dickinson: A Child with a Tail. Brooklyn Medical Journal, vol. viii, 1894.

Halsted Myers: A Caudal Appendage. Proceedings of the New York Pathological Society, (1893) 1894.

Julian Berry: Baby with a Tail. Memphis Medical Journal, vol. xiv, 1894.

A. Ecker: Der Steisshaarwirbel (vertex coccygeus), die Steissbeinplatte (glabella coccygea) und das Steissbeinrübchen (foveola coccygea), wahrscheinliche Ueberbleibsel embryonaler Formen, in der Steissbeinegend beim ungeborenen, neugeborenen und erwachsenen Menschen. Archiv f. Anthropol., Bd. xii, 1880. Ecker describes a case reported to him in a letter from Dr. Neumayer, of Cincinnati.

Miller: Medical and Surgical Reporter, 1881. (Not accessible.)

⁸ Archiv f. Anthropol. Bd. xx, p. 219.

⁹ M. Bartels: Ueber Menschenschwänze. Archiv f. Anthropol., Bd. xiii, 1881. In this paper Bartels classifies persistent tails, dividing them into two main types, adherent and freely suspended (*freie*); of the latter

cases in which the tail projects free from the trunk as, for instance, cases described by Braun,¹⁰ Ornstein,¹¹ and by Dickinson. The majority of the embryonic tails contain, however, no prolongation of the vertebral column but are classed as what Virchow¹² calls soft tails (*weiche Schwänze*).

DESCRIPTION OF CASE.

About a year ago Dr. Watson exhibited before the Johns Hopkins Hospital Medical Society a baby with a tail, which is an example of the last-named class.¹³ The tail was removed later, and through the kindness of Dr. Watson, who gave me the specimen as well as his notes of the case, I am enabled to make a fairly complete report on it, including a description of its histological structure.

The child, which was the third in the family, was a healthy, well-developed male. In its family history there is nothing which throws any light upon the case. Aside from the tail the baby presented only one other slight deformity, and that was in the four outer toes of the right foot. These toes were shorter than the normal ones of the left foot, their tips were turned up and the nails were small and thick. The phalanges of these toes were short and there were but two in each toe. The great toe of this foot was normally developed.

The tail appendage was attached in the mid-line about one centimeter below the tip of the coccyx. Examination of the sacro-coccygeal region showed a well marked *foveola coccygea* (Ecker) (Figs. 1 and 2), but owing to the extreme fineness of the hairs of this region, which to the unaided eye were quite invisible, it was impossible to distinguish any particular coccygeal bald spot or *glabella coccygea* (Ecker). Beginning a little to the right and below the *foveola* is a sharply defined groove, which runs obliquely downward and to the left between the buttocks and passes to the left of the root of the tail.

The appendage itself was of firm consistency, though containing no bone. It was covered with normal skin, containing fine hairs; and was apparently well vascularized. Three distinct portions or segments could be made out. The basal piece was short and on the dorsal side scarcely marked off from the next following, except when the tail was in a state of contraction (Fig. 2). On the ventral side a transverse furrow separated it from the next portion. The middle segment had a length of 25 mm., was curved a little to the right and tapered somewhat towards its distal end, where the much more slender end-segment was attached. These two portions were separated by a constriction more marked on the left side.

a number of subdivisions are made, between which, however, the distinction does not seem to me to be sharp.

¹⁰ M. Braun: Ueber rudimentäre Schwanzbildung bei einem erwachsenen Menschen. Archiv. f. Anthropol., Bd. xiii, 1881.

¹¹ Ornstein: Schwanzbildung beim Menschen. Archiv f. Anthropol., Bd. xiii, 1881.

¹² R. Virchow: Schwanzbildung beim Menschen. Deutsche med. Wochenschr., 10. Jahrg., 1884.

¹³ W. T. Watson: Exhibition of a Three-months' Infant with a Caudal Appendage. Proc. J. H. H. Med. Soc. Johns Hopkins Hospital Bulletin, vol. xi, 1900.

The terminal segment curved to the right and ventrally and ended in a rounded blunt extremity. On the whole, the tail gave an impression not unlike that of a pig's tail, a similarity which has been noted in a number of cases previously reported.

The hairs upon the tail, which were considerable in number, were plainly visible to the unaided eye. They pointed towards the tip, as could readily be confirmed by examination of longitudinal sections (Fig. 4). The convergence of the hairs towards the tip of the tail corresponds with the arrangement of the hairs in the coccygeal whorl (*vertex coccygeus* of Ecker), found in normal, *i. e.* tailless individuals, and supposed to be a vestige of the embryonic tail.

Two weeks after the birth of the child the tail was 4.4 cm. long; at the age of two months it had grown to 5 cm.; and at six months, when it was removed, it had attained the length of 7.0 cm., showing altogether a fairly rapid rate of growth.

The most remarkable characteristic of the tail was its movability. When at rest it would lie extended in the mid-line (Fig. 1), or bent over to one side upon the buttocks. The mother of the child said that she had seen the tail bent through an angle of 180°, its tip pointing towards the head. It must, however, have been brought into this position passively, for, as will be seen later, there was nothing in the arrangement of its muscles which could account for this. When the child was irritated, and cried or coughed, the tail would contract markedly. Between the basal and middle segments but little movement was possible; the contraction of the muscles merely brought out the constriction between the two portions more plainly. Between the middle and distal segments the movement was considerable. The latter could be drawn in sharply, telescoping the middle segment, and at the same time flexion to the left side took place. During this action the middle segment became much shorter and thicker.

When the child was about six months old the tail was removed by Dr. Watson.¹⁴ The amputated appendage was put immediately into Zenker's fluid to harden. After it had been washed and kept in strong alcohol for some time it measured 5.3 cm. in length. It was then cut into four pieces with a sharp razor, and the pieces were imbedded in celloidin. Cross sections were cut at three different levels, near the base, proximal to the second joint, and near to the tip, as is indicated in Fig. 4. After a few transverse sections were cut off, the pieces were stuck together and reimbedded in celloidin for the purpose of cutting longitudinal sections of the whole.

From the study of sections it is seen that the skin covering the whole of the tail except a limited area on the ventral sur-

¹⁴ It seemed advisable to remove the tail, not only in order to accede to the wishes of the child's parents, who regarded its presence with chagrin, but also on more practical grounds. It looked as if the tail might become the seat of a troublesome intertrigo. Besides, its rate of growth was considerable, and it did not seem unlikely that the appendage might have later attained undue proportions, causing, as has been reported in several instances, considerable inconvenience in sitting. (See Lissner: Virchow's Archiv, Bd. 99, 1885.)

face is of normal structure. The layers of the epidermis are easily distinguishable. The thickness of the skin varies somewhat. Near the base of the tail on the ventral side it is found to be quite 2 mm. thick, while on the dorsal surface of the same portion it is scarcely 1.5 mm. Further out, *i. e.* at the middle cut (Fig. 4, *a*), there is the same difference in thickness between skin of the ventral and dorsal surface (Fig. 5), although the skin is here not quite so thick as at the base. Near the tip the thickness throughout the whole circumference is nearly 1.5 mm. The greater thickness of the skin on the ventral side at the base is due principally to the epidermis, the corium being more nearly uniform throughout. In the thickened area the epidermal ridges extend down deep into the cutis, and the papillæ are very long and slender. The various integumentary organs, sweat glands, sebaceous glands and hairs, are numerous and of normal build. In longitudinal sections (Fig. 4) it may be very plainly seen that the hair follicles are obliquely inserted, the hair pointing towards the tip of the appendage. This is without exception the case in the proximal two-thirds of the tail, although the regular arrangement is somewhat disturbed at the crease where the distal and middle segments join, especially on the left side. The corium contains a very abundant supply of elastic fibres which may be readily demonstrated in sections stained by Weigert's method.

Beneath the skin the main bulk of the tail is made up of areolar tissue containing much fat. Blood-vessels, nerves, and striated muscle fibres are imbedded in this mass. There is no trace of anything like the medullary cord or of notochordal tissue, as Gerlach found in the tail of a fœtus of four months.

The voluntary muscle consists of a few bundles of fibres which take origin from the subcutaneous areolar tissue near the proximal end of the middle segment. They lie on the left side not far from the mid-line (Figs. 4 and 5), and run distally in parallel bundles diverging somewhat towards their insertion in the skin just beyond the joint between the middle and distal segments. The majority of the fibres are attached on the left side; a few, however, pass to the skin of the right side; and others are attached to the dorsal surface, and perhaps a few ventrally. The action of the muscle is thus clearly explained by its anatomical relations. There are no muscle fibres running between the trunk and the tail.

On the right side near the middle of the tail there are a few muscle fibres (Fig. 5, *M'*), but these are isolated in small bundles or as single fibres by a dense stroma of connective tissue. Moreover, nearly all of these fibres are in a state of degeneration. The fibrils are less distinct than usual, and the nuclei may be found scattered throughout the substance of the fibres. The muscle is, in fact, in an advanced stage of simple atrophy.

No one of the blood-vessels stands out preëminently in size. The largest artery is on the left side, held in place by strong connective-tissue bundles. This may be seen in sections through the middle (Fig. 5, *A*), as well as through the base of the tail. There are several smaller vessels in the

vicinity. Two small arteries are seen in the right dorsal quadrant near the centre and one just beneath the corium, to the left of the mid-line. The veins are small and inconspicuous. There is nothing to be seen of a tuft-like branching of the vessels as Virchow¹⁵ describes in one of his cases, nor is there anything resembling erectile tissue.¹⁶ There is, however, an abundant supply of blood-vessels in the corium.

A number of small nerve trunks (Fig. 5, *N*) run longitudinally in the areolar tissue of the appendage. The majority of these accompany blood-vessels.

Similar Cases.—While it is not practicable to enumerate here all of the similar cases which have hitherto been reported, there are some which for one reason or other are of especial interest. The tail of a Moï,¹⁷ ten years of age, which had attained the length of over twenty-five centimeters, is interesting on account of its size. Many of the cases have been described very briefly and only as regards external appearance. There are, however, a number of cases which have either been dissected or examined microscopically. These include Greve's case described by Virchow,¹⁸ and cases reported by Meyers,¹⁹ Vinogradow,²⁰ Rodenacker²¹ and Scheboldayeff,²² all of which agree with the present case in general structure but differ from it in the absence of muscle. In two other cases, however, described by Pyatnitzki²³ and Gerlach,²⁴ respectively, striated muscle fibres were found, and it is to be assumed that such tissue was present in Neumayer's case, for the tail in this instance could be excited to reflex contraction by stimulation of the sacral region. The complicated arrangement of the muscles found in some instances is associated with the occurrence of bone, as in the case described by Hennig and Rauber,²⁵ and especially in Kohlbrugge's case.²⁶ The tail described by Gerlach in a fœtus of 4.6 cm. also contained a continuation of the notochord, which has as yet never been seen in older subjects.

THE TAIL IN THE HUMAN EMBRYO.

The caudal region in human and other mammalian embryos has already been described by Ecker, His, Keibel, Fol, Braun and others. These accounts, while agreeing in the main, bring out considerable differences of opinion as to details. For this reason I give here a further description of the tail

¹⁵ Virchow's Archiv, Bd. 79, 1880.

¹⁶ Bartels: Archiv f. Anthropol., Bd. xv, p. 116.

¹⁷ Caudal Appendage in Man. (From the French of Étienne Rabaud, in "La Naturaliste.") Scientific American, vol. 50, 1889.

¹⁸ Virchow's Archiv, Bd. 79, 1880.

¹⁹ Proc. N. Y. Pathol. Soc., 1893.

²⁰ K. N. Vinogradow: On Human Tails. Vrach, vol. xv, 1894 (Russian).

²¹ G. Rodenacker: Ueber den Säugethierschwanz mit besonderer Berücksichtigung der caudalen Anhänge des Menschen. Inaug.-Diss., Freiburg i. Br., 1898.

²² W. Scheboldayeff: Tailed Men. Zemsk. Vrach, vol. vi, 1893 (Russian).

²³ Inaug.-Diss., St. Petersburg, 1893.

²⁴ L. Gerlach: Ein Fall von Schwanzbildung bei einem menschlichen Embryo., Morphol. Jahrb., Bd. vi, 1880.

²⁵ C. Hennig and A. Rauber: Ein neuer Fall von geschwänztem Menschen. Virchow's Archiv, Bd. 105, 1886.

²⁶ Natuurkund. Tijdschr. v. Ned. Indië, Deel. lvii, 1898.

region in several human embryos. This I am enabled to do through the kindness of Dr. Mall, who placed at my disposal his fine collection of human embryos. Two specimens, fourteen and sixteen millimeters long respectively, were found to be especially adapted for this purpose, for it is at this stage that the tail reaches the highest point in its development. The study of these was greatly facilitated on account of their excellent state of preservation, and by the fact that they were cut into perfect series of sagittal sections.

Embryo 144. Greatest Length 14 mm.; Neck-Breech 12 mm.—The tail of this embryo is marked off ventrally by a fold of epithelium which extends cranially from the anus, forming a shallow pit or crease between the anal prominence and the tail. This fold extends to the level of the cranial end of the thirty-third vertebra (Fig. 6), so that from this point on, *i. e.* distal to the third coccygeal vertebra, the caudal end of the embryo projects free from the trunk.

The vertebral column extends throughout but half the length of the tail, in which, therefore, a vertebral and non-vertebral portion may be distinguished.

The terminal portion of the tail or caudal filament is bent dorsally and inclined to the left side, and becoming rapidly thinner distally, ends in a slight knob-like enlargement, which is scarcely shown in the figure. The most conspicuous structure in the caudal filament is the medullary cord, which runs to the tip and there ends in a vesicular enlargement. The notochord and the terminal branches of the aorta and inferior vena cava also extend out into it though not so far as the medullary cord. The filament is supported by a diffuse mesenchymatous network, more concentrated in the ventral side just beneath the integument, which is perhaps an indication of the remains of the post-anal gut found in younger embryos.

Counting from the atlas down, it is clear that there are in all thirty-six vertebrae present, of which the distal seven belong to the coccygeal or caudal region. In the trunk, down through the sacral region, the vertebral bodies are composed of embryonic cartilage, which does not stain intensely. The intervertebral discs, owing to the greater concentration of the cells composing them, stand out in sections as deeply staining bands. Between the vertebral bodies and the discs there is a zone of cells, which stains more intensely than the cartilage and less so than the discs. In the well advanced vertebrae of the lumbar region the intermediate zone is thin and clearly forms a part of the perichondrium of the vertebral cartilages. Beginning with the first coccygeal vertebra this intermediate or perichondrial layer forms a thick pad, especially on the distal surface of the disc. The vertebral body is here proportionately thin, showing itself merely as a lighter streak between the more deeply staining perichondrium of each end. In fact the bodies of the distal coccygeal vertebrae can hardly be spoken of as cartilaginous. In thickness (cranio-caudal) the vertebral bodies diminish steadily throughout the sacral and coccygeal regions, but there is very little diminution in the dorsoventral diameter until the thirty-fourth vertebra is reached. The last three diminish rapidly towards the

tip. In the last two the discs are fully as thick as the vertebral bodies themselves. The distal surface of the vertebra is capped by a well marked disc. There is on each side of the intervertebral discs in the coccygeal region a small mass of deeply staining tissue, which projects ventrally and laterally. They are visible only in sections which pass to the side of the mid-line. They represent undoubtedly rudimentary hypapophyses or haemal arches found in the caudal vertebrae of lower forms.

The spinal ganglia, not counting the ganglion of the hypoglossus, are thirty-three in number. In connection with the last a distinct ventral ramus arises and passes ventrally to the side of the vertebrae, bending distally; ventral to the vertebrae it joins a trunk from the next higher nerve. Its mode of ending is uncertain.

The number of muscle plates could not be made out clearly.

In the interval between the thirty-first and thirty-second vertebrae the medullary cord (*med.*) becomes suddenly attenuated into a *filum terminale*. There are apparently few or no neuroblasts beyond this point; the walls of the tube are made up of columnar epithelial cells. In the distal portion of the vertebral region and at the base of the caudal filament the cord takes a somewhat sinuous course. The central canal extends to the tip of the tail, where it ends in the slight enlargement mentioned above, the terminal ventricle.

The notochord (*ch.*) forms the axis of the vertebral bodies and discs, and in the proximal portion of the coccygeal region, as in the trunk, is almost straight. In the region of the last two or three vertebrae it is more tortuous. It leaves the vertebral column near the dorsal surface of the last vertebral body and passes thence dorsally to the ventral side of the medullary cord, accompanying this nearly to the tip. In contrast to the vertebral portion, the terminal portion is scarcely differentiated and not well defined in the surrounding mesenchyme.

The continuation of the aorta (*ao.*), *i. e.* the *a. sacralis media*, at first ventral to the vertebrae, passes out into the caudal filament as an *a. caudalis*. From this are given off the segmental arteries, one for each vertebra down to and including the last or thirty-sixth. (The last two are not shown in the figure.) These pass up on each side of the vertebral bodies, but it is doubtful if the more distal ones are as yet fully open. In the same way the vena cava continues into the tail, as the *v. sacralis media* and the *v. caudalis*, which lies ventral and to the right of the artery. At their termination in the caudal filament the artery and the vein meet. The vein is of large calibre to the region of the thirty-second vertebra; here it narrows down very suddenly. There are numerous small blood-vessels throughout the mesenchyme of the tail.

Embryo 43. Greatest Length 16 mm.; Neck-Breech Length 14 mm.—The relations of the tail to the trunk are about the same as in the younger embryo first described, *i. e.* it is free from the thirty-third vertebra on.

The vertebral portion of the tail is longer, but the caudal

filament is shorter and more shrunken. It bends sharply on itself to the dorsal side, almost through an angle of 180° .

Thirty-seven vertebrae are present, with possible indications of a thirty-eighth; eight of these belong beyond doubt to the coccygeal region. The thirty-fourth and thirty-fifth are partly fused in the middle. The hypapophyses of each are distinct.

The spinal ganglia number thirty-two. The relations of the notochord, medullary cord and blood-vessels are the same as in the embryo first described. There is a slight irregularity in the notochord in the form of a process which extends ventrally into the substance of the thirty-sixth vertebra.

GENERAL CONSIDERATIONS.

Ecker²⁷ and His²⁸ were the first to give detailed descriptions of the caudal region of the human embryo. Their conclusions regarding its definition and ultimate development may be taken as the starting point in the discussion of the subject. The agreement reached by Ecker and His may be rendered in part as follows:²⁹ (1) The term "tail" may be applied only to that portion of the embryo which projects free beyond the cloaca. (2) The tail consists of a portion containing vertebrae and a portion without vertebrae (caudal filament). The latter contains only notochord and medullary cord. (3) Only the non-vertebral portion atrophies. The vertebral portion remains for some time as the coccygeal prominence (*Steisshöcker*), which, however, gradually disappears in consequence of the increase in the curvature of the sacrum and coccyx, and of the progressive development of the pelvic girdle and its musculature.

Two matters which have a bearing upon the morphological significance of the persisting caudal appendages in man are brought up in the above for consideration. The one concerns the structure of the tail in the human embryo in comparison with the tail in lower forms; the other is the nature and amount of regressive change which takes place in the human tail during development.

Regarding the first, Keibel³⁰ discovered an additional fact of importance in the presence of a post-anal gut in the human embryo. Braun's³¹ observations on the caudal filament of mammalian and bird embryos are of importance in showing that the caudal filament is of general occurrence and not a peculiarity of the human tail. Again, the occurrence of spinal nerves and ganglia in a number of the coccygeal seg-

ments, as shown by Fol,³² Phisalix³³ and Keibel, the continuation of the aorta and vena cava into the caudal filament, together with the presence of segmental arteries and the hypapophyses or rudimentary hæmal arches in all of the coccygeal segments as described in the present paper, show that the caudal region of the human embryo resembles that of other mammalian embryos in all respects except in size and in the number of its segments.

Concerning the regressive development of the tail considerable difference of opinion has been expressed. Rosenberg, who holds that, strictly speaking, the caudal rudiment in man is not the homologue of the tail of other animals, but is the result of a precocious growth of the medullary cord,³⁴ considers that the appendage disappears in consequence of the increase in volume of that end of the embryonic body and not through absorption. His,³⁵ in supporting Rosenberg, makes the statement that no reduction in the number of segments takes place during the development of the human embryo, but that the regressive changes are confined to the caudal filament: this view is confirmed in the agreement with Ecker. On the other hand, Fol and Phisalix find thirty-eight segments in embryos of 8-10 mm., with indications that several of these disappear through fusion in the course of development. Allowing for the possibility that these observers have counted in an occipital segment, there would be in embryos of this size at least thirty-seven trunk segments, which would correspond to thirty-six vertebrae. Keibel finds in an embryo of 8 mm. thirty-five trunk segments, together with a mass of unsegmented mesoderm, equaling two segments in length. Reckoning this as two instead of one segment, as Keibel does, we have again thirty-seven segments, corresponding to thirty-six vertebrae.

The following is an attempt to tabulate the number of segments found in embryos varying in length from 7.5 to 21.5 mm. With the exception of the last column the data are as recorded by the observers themselves. In the last column the number of vertebrae is given which would correspond to the total number of segments after certain changes have been made, such as deduction of occipital segments or addition of unsegmented mesoderm, which seemed justified by the descriptions of the authors.

³² H. Fol: Sur la queue de l'embryon humain. Comptes Rendus, T. 100, Paris, 1885.

³³ C. Phisalix: Étude d'un embryon humain de 10 millimètres. Archives de Zool. Exp. et Gén. II^{me} S., T. vi, 1888.

³⁴ E. Rosenberg: Ueber die Entwicklung der Wirbelsäule und das centrale earpi des Menschen. Morphol. Jahrb., Bd. i, 1876. "... dass die Gestaltung des hinteren Leibesendes ebenfalls von dem Medullarrohr derart beeinflusst wird, dass letzteres, indem es in seinem Längenwachsthum dem der anderen, in der Zusammensetzung des hinteren Leibesendes Theilhabenden Bestandtheile voraussetzt, an demselben einen Vorsprung erzeugt. . . ." p. 128.

³⁵ "Es werden demnach beim menschlichen Embryo keine überzähligen zur Rückbildung bestimmten Segmente angelegt." Anatomie menschlicher Embryonen, i, p. 92.

²⁷ A. Ecker: Archiv f. Anthropol., Bd. xii, 1880.

A. Ecker: Besitzt der menschliche Embryo einen Schwanz? Archiv f. Anat. u. Physiol. anat. Abtheil., 1880.

²⁸ W. His: Anatomie menschlicher Embryonen, 1, Leipzig, 1880.

W. His: Ueber den Schwanztheil des menschlichen Embryo. Archiv f. Anat. u. Physiol. anat. Abtheil., 1880.

²⁹ A. Ecker: Replik und compromissitze nebst Schlusserkärung von W. His. Archiv f. Anat. u. Physiol. anat. Abtheil., 1880.

³⁰ Fr. Keibel: Ueber den Schwanz des menschlichen Embryo. Archiv f. Anat. u. Physiol. anat. Abtheil., 1891.

³¹ M. Braun: Entwicklungsvorgänge am Schwanzende bei einigen Säugethieren mit Berücksichtigung der Verhältnisse beim Menschen. Archiv f. Anat. u. Phys. anat. Abtheil., 1882.

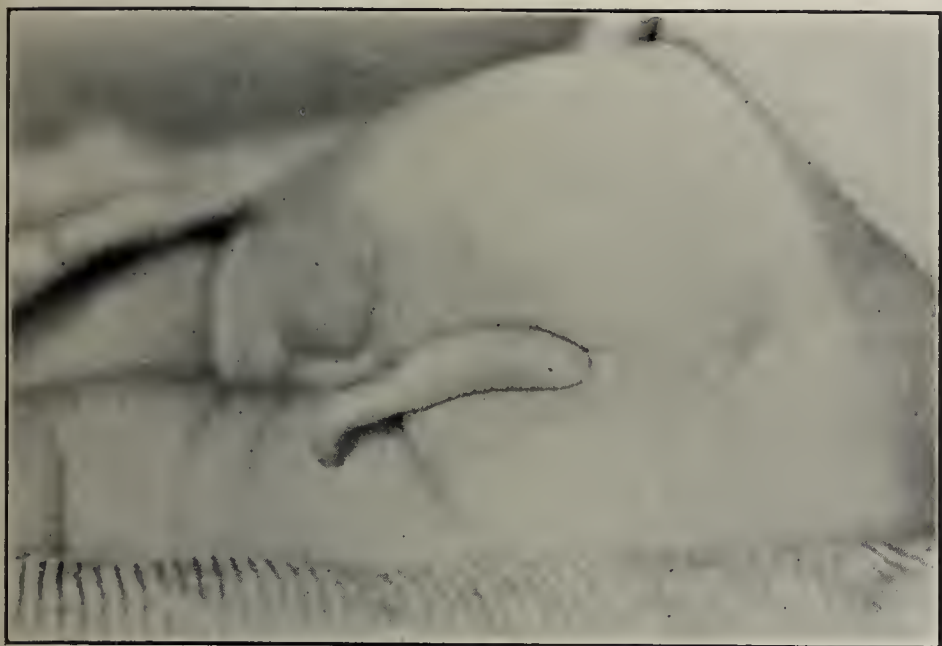


FIG. 1.—Photograph showing tail in extended condition.



FIG. 2.—Photograph showing tail in state of contraction.



FIG. 3.—Photograph showing the ventral surface of tail.

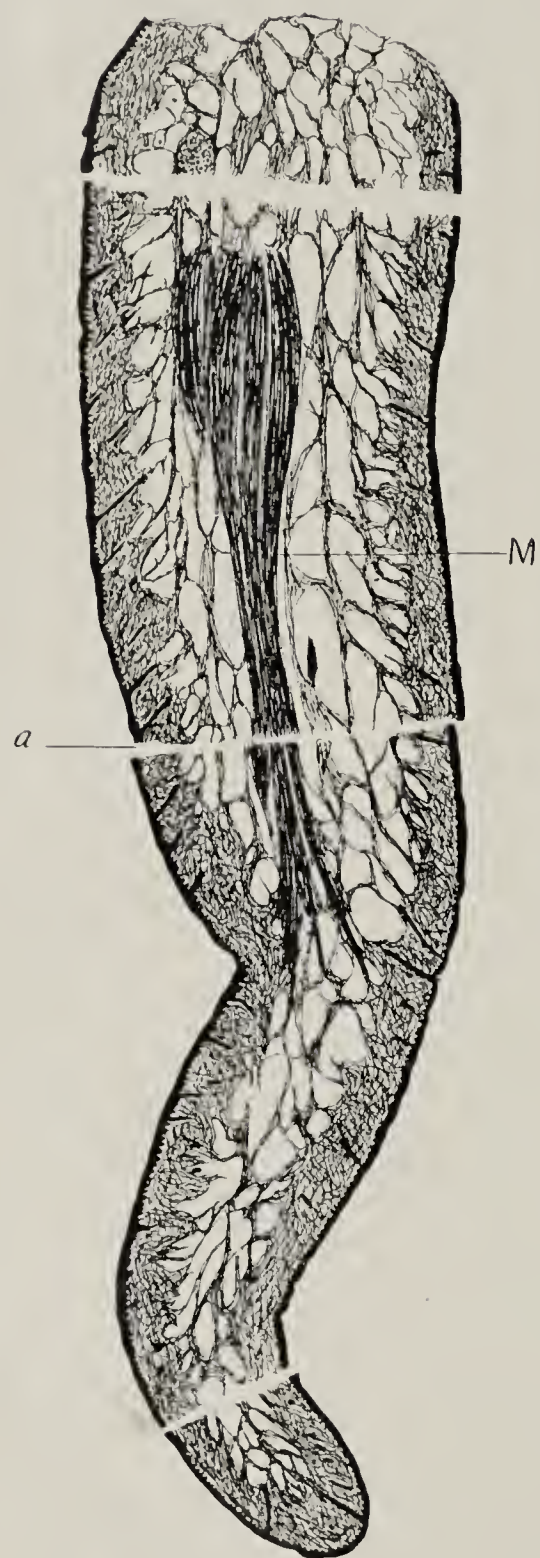


FIG. 4.—Frontal sections of tail, showing the arrangement of the muscle fibres (*M*). *a*, Place from which the cross-section represented in Fig. 5 was taken. $\times 3$.



FIG. 5.—Cross-section through the middle of the tail (Fig. 4, *a*). *M*, muscle; *M'*, degenerating muscle; *A*, artery; *N*, nerve; *L* is placed on the left and *R* on the right of the appendage. $\times 9$.

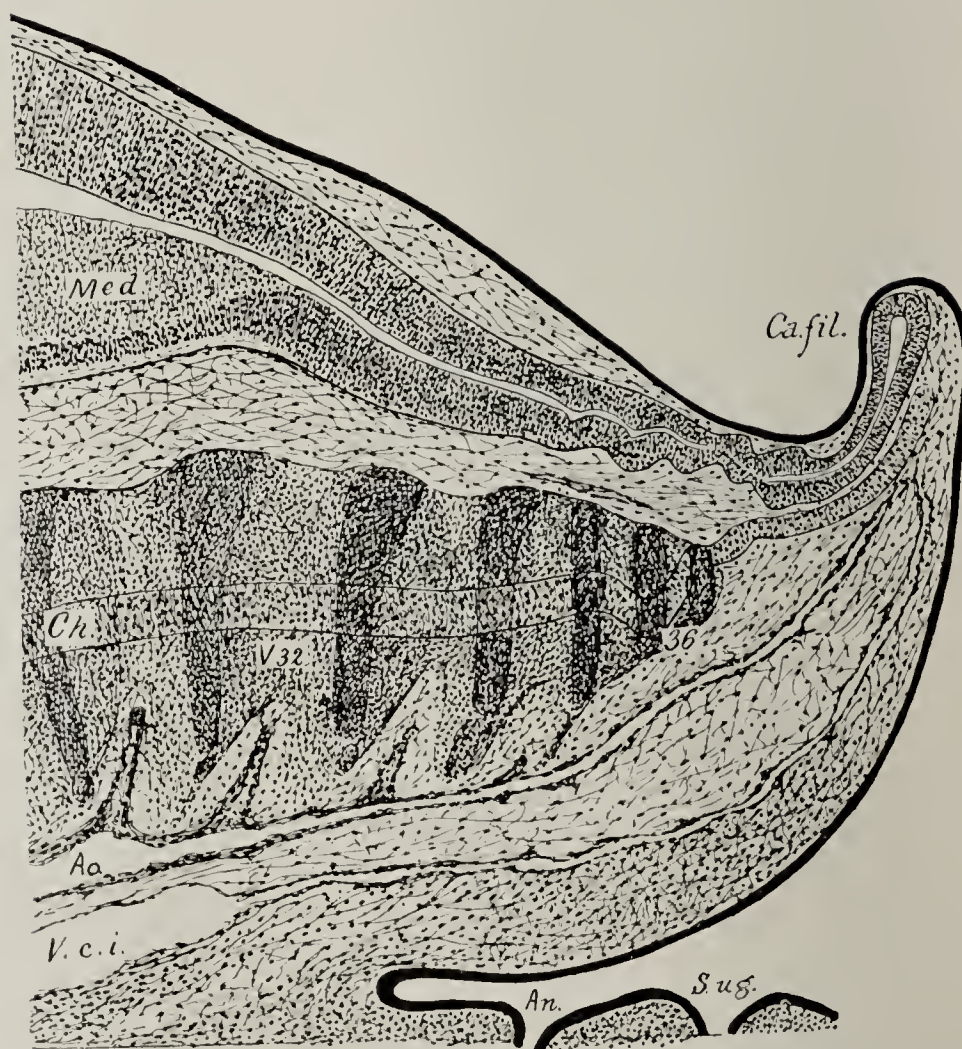


FIG. 6.—Caudal region of embryo of 14 mm. (No. 144 of Dr. Mall's collection), combined from several sagittal sections. *An.*, anus; *Ao.*, caudal aorta (*A. sacralis media*); *Ca. fil.*, caudal filament; *Ch.*, notochord; *Med.*, medullary cord; *S. ug.*, sinus urogenitalis; *V. 32*, third coccygeal vertebra; *36*, seventh coccygeal vertebra; *V. c. i.*, caudal portion of *vena cava inferior* (*V. sacralis media*). $\times 91$.

Observer.	Length of embryo in mm.	Segments in mesoderm.	Spinal ganglia.	Vertebrae.	Corresponding number of vertebrae after allowing for corrections.
His	7.5	35	—	34	34
Keibel.....	8.0*	35 + unsegmented mesoderm.	—	—	36†
Fol.....	8.0-9.0	38	—	36	36
Phisalix	10.0	38	36	..	36
Keibel.....	11.5*	35 + unsegmented mesoderm.	34	35	36†
Fol.....	12.0	..	—	36	36
Harrison ...	14.0	..	33	36	36
Harrison ...	16	..	32	37	37
His	16.0	34	34
Rosenberg..	16.5	33	33
Fol.....	19.0	34	34
Rosenberg..	19.0	35	35
His	21.5	34	34

* Neck-breech measurement.

† Counting the terminal mesoderm as equivalent to two segments.

From this it may be seen that the number of vertebrae or their equivalent is fairly if not quite constant in embryos between eight and sixteen millimeters in length. We have, then, seven vertebrae in the embryonic tail at its highest period of development. The stages studied by His and by Rosenberg were either too young or too far advanced to show the maximum number of vertebrae. That the reduction takes place by fusion, as is maintained by Fol, is confirmed by the study of the embryos described above. In the older embryo (16 mm.), in which an exceptionally large number of segments was present, partial fusion between several of the adjacent vertebrae had taken place. In still older embryos, as seen in the table, the number of segments is inconstant; most probably this is due to the varying extent to which fusion has taken place, though it is possible that it may be due in part to a difference in the original number. As Steinbach³⁶ shows, the usual number of segments is thirty-four, *i. e.* five coccygeal, although the number may be less or, in rare instances, even increased by one.

The spinal ganglia of the caudal region, as Keibel has shown, also suffer reduction. There are never quite so many ganglia developed as vertebrae, and the last ones are always more or less rudimentary; but there are always more formed than persist in the adult. For instance, in an embryo of 10 mm. Phisalix described thirty-six ganglia; in an embryo of 11.5 mm. Keibel found thirty-four; in the embryo of 14 mm. described above there were thirty-three, and in the embryo of 16 mm. thirty-two, while in the adult there are but thirty-one. The segmental arteries of the distal caudal segments also become obliterated as development proceeds.

We conclude, then, with Keibel that, while as far as outward form is concerned the embryonic tail disappears largely as a result of the growth of the extremities and the gluteal region, a certain amount of regressive change takes place in the caudal appendage itself. This is manifest not only in the

absorption of the caudal filament, as supposed by Ecker and His, but also in the reduction of all essential structures of the vertebral portion of the tail, *i. e.* the vertebrae, muscle segments, spinal ganglia and blood-vessels. It is interesting to note that in this tendency to reduction the resemblance between human and other mammalian tails also holds. The caudal filament, as Braun has shown, is present in other embryos and atrophies as development proceeds. The tendency to fusion of the distal vertebrae has been observed in the embryos of various long-tailed animals. And in short-tailed varieties, as Bonnet has shown, this tendency is merely accentuated.³⁷

The view that a great many of the anomalous caudal appendages found in man are, as stated in the beginning, due to the persistence of the embryonic tail, is warranted by the facts gathered both from the study of the former as well as of the latter. Many of the differences in form are explained by the hypothesis of Bartels that the embryonic tail may be arrested in any stage of its development. The soft or boneless tails are clearly not due to the multiplication of vertebrae or even to the persistence of all which are developed in the embryo, but, as His³⁸ first suggested, are to be regarded as persisting caudal filaments. The usual position of these appendages as well as their structure support this conclusion. The fact that they are not always attached exactly over the tip of the coccyx cannot be regarded as conflicting with this view, for, as has long been recognized, the curvature in the vertebral column, especially in the sacral and coccygeal regions, changes markedly during development, and the caudal filament not being firmly united to the tip of the coccyx might easily be shifted slightly in relation to the latter.

In the action of amniotic adhesions Schaeffer³⁹ has suggested a cause which may undoubtedly bring about the persistence of the caudal filament, for it is a fact that in many, perhaps in a majority of the cases there are other evidences of such adhesions having been present, and, as Schaeffer points out, the caudal region, like other projecting portions of the embryo, is especially liable to stick to the amnion. The adhesions are to be regarded, however, merely as a factor which may induce the persistence of an otherwise transitory structure and it does not follow that such persistence is always the result of adhesions. On the contrary, we find in certain animals that the caudal filament normally persists. According to Braun, this is probably the origin of the tail-stump, composed of areolar tissue, found in *Inuus pithecus*, and similar appendages are also found sometimes in the Chimpanzee, as Rosenberg has described.

³⁷ R. Bonnet: Die stummelschwänzigen Hunde im Hinblick auf die Vererbung erworbener Eigenschaften. Zeigler's Beiträge z. path. Anat. u. allg. Pathol., Bd. iv, 1889.

³⁸ Anatomie menschlicher Embryonen, i, p. 95.

³⁹ Archiv f. Anthropol., Bd. xx, 1892, p. 219.

³⁶ E. Steinbach: Die Zahl der Caudalwirbel beim Menschen. Inaug. Diss., Berlin, 1889.

DEVELOPMENT OF THE PIG'S INTESTINE.

BY JOHN BRUCE MACCALLUM, M. D.,

Assistant in Anatomy, Johns Hopkins University.

By the work of Henke¹ and of Weinberg² it was first shown that the various parts of the human intestine hold a definite relative position in the body. But it was not until 1897, when the researches of Mall³ were published, that this subject was put on a satisfactory basis. Professor Mall described in detail the development of the human intestine, the protrusion of loops into the coelom of the umbilical cord and their return to the general body-cavity. He traced the various loops through different stages in their development and showed that in the human adult these loops are massed together into definite groups, which maintain a constant position in the abdominal cavity.

Merkel,⁴ in his handbook, has considered all the literature on the subject and has given a description of his own work, the results of which are in accord with those of Mall.

Dexter⁵ has lately described the development of the intestine of the cat. He finds no definite arrangement of the intestinal loops to be present in this animal.

The following notes were made in the study of a considerable number of pig's embryos:

METHODS AND MATERIAL.

In this study there was used a series of pig's embryos varying in length from 12 mm. to 12 cm. An attempt was made to obtain embryos with each stage, showing only the least possible advance on the one preceding it. In some stages several embryos from the same uterus were examined in order to determine the constancy of the loops of intestine in individuals of the same age. Types chosen from the various large groups of lower animals were also studied.

The only method used was one of direct dissection. The embryos were hardened in formalin or alcohol, which rendered the intestines firm and not easily displaced. The abdominal cavity was opened and the liver carefully lifted away and dissected out under water. The Wolffian body and kidney were similarly removed. The umbilical cord was then laid open to expose that part of the coelom which it contained. In this way the intestines could be well isolated without disturbing them in the least. Starting, then, with the stomach the various loops were followed and modeled with copper wire. This could be bent so as to accurately represent the direction of each loop, and the general position of the loops of wire could be constantly compared with that of the intestinal loops, so that very little error could arise. On reaching the anus

the whole intestine was gone over again starting with the rectum and ending in the stomach. In this way any error could be well controlled. The whole model was then compared again with the embryo to see that the surface coils corresponded. To aid in drawing and studying these models the various groups of coils were painted in different colors. The same method was employed in the study of the lower animals. In the simpler types, however, the wire models were unnecessary. In the earliest embryos also the arrangement could be made out perfectly well without modeling.

DESCRIPTION OF DISSECTIONS.

Until the embryonic pig has reached a length of about 40 mm. there is in every case some part of the intestine in the umbilical cord. The portion nearest the stomach develops entirely outside the cord; while what corresponds with the lower end of the ileum, together with the cœcum and a short stretch of the large intestine, remain in the cord until the stage mentioned above. The part in the neighborhood of the cœcum is the last to leave the cord. All the loops which develop within the cord belong to the part of the intestine corresponding in position with the lower end of the ileum. This develops more slowly than the intra-abdominal portion of the gut.

In the following descriptions the terms "right" and "left" refer to the pig's body and not to the figures themselves. "Anterior" and "posterior" refer to the head and tail ends respectively; while the terms "dorsal" and "ventral" are used in their ordinary sense. The figures are all drawn from the right side of the embryo's body unless otherwise indicated.

Figure 1 represents an early stage in the development of the pig's embryo, in which the intestine consists of a single loop extending out into the umbilical cord. The embryo itself is 12 mm. long and the loop in the cord is slightly less than 3 mm. in length. This loop is somewhat curved with the concave surface towards the head. As represented in Fig. 1 the intestine is sharply bent on itself in the cord, and on its return to the main body-cavity it turns at an acute angle to form the rectum. I can discover no trace of a cœcum at this stage other than a slight enlargement of the tube just after it bends in the cord. The arm of the loop which extends from the stomach into the cord is destined to give rise to the small intestine; while the arm returning from the cord to the rectum is, roughly speaking, the forerunner of the large intestine. Several embryos of this size were examined, and the condition described above found to be constant.

In Fig. 2 there is shown the dissection of a pig's embryo, 18 mm. in length. The loop of intestine extending into the cord is much like that represented in Fig. 1. A distinct cœcum, however, can be made out in the rectal arm of the

¹ Henke; *Arch. f. Anat. und Phys. Anat. Abth.*, 1891, S. 89.

² Weinberg; *Internat. Monatsch. f. Anat. und Phys.*, xiii Bd., 1896.

³ Mall, F. P.; *Arch. f. Anat. und Entwicklung. Anat. Abth. Supplementband*, S. 403, 1897; and *Anatom. Anz.* Bd. 16, S. 492, 1899.

⁴ Merkel; *Handbuch der Topographischen Anatomie*, ii Bd., 1899.

⁵ Dexter, F.; *Arch. f. Anat. und Phys., Anat. Abth.*, 1899.

loop, a short distance from where the intestine bends on itself. This cœcum is a short blind sac having an appearance very much like that shown in the figure. It will be noticed that a considerable part of the body-cavity is, in this stage, in the umbilical cord. Fully half the length of the intestine is contained in this extra-abdominal cœlom. Just inside the main body-cavity a loop is beginning to be formed in the small intestine. Its bends are marked 1, 2 and 3. From the stomach it extends dorsally and to the right. Turning sharply it runs ventrally and to the left, and before entering the cord it proceeds again posteriorly. On comparing Figs. 1 and 2, there is seen a greater change in this part of the intestine near the stomach than in the part contained in the cord. The large intestine beginning at the cœcum turns and passes into the rectum as before. Several embryos of this size showed an identical structure.

Fig. 3 represents a pig 21 mm. long. The portion of the intestine in the cord is still unchanged, while that in the body-cavity proper shows a further development of the same loops seen in Fig. 2. In comparing the numbers on the two figures there is no difficulty in recognizing the corresponding parts. The cœcum holds the same relative position as in Fig. 2. After entering the cord at the loop 3 in Fig. 3 the intestine bends in a curve with the concave side towards the head. It then turns abruptly backward and to the left, and returns to the main body-cavity by almost the same path. This is represented plainly in Fig. 3, and it will be noticed in the succeeding stages that this particular arrangement of the intestine as it turns is quite characteristic.

Fig. 4 shows a somewhat more advanced stage in the development. It is drawn from the dissection of a pig 23 mm. long. The general position of the intestine is very similar to that just described. The loops, however, have increased in number; and instead of one entire loop, as represented in Fig. 3, there are three, indicated by the letters *a*, *b* and *c* in Fig. 4, *B*. In Fig. 3 the stomach narrows into the small intestine, which bends rather abruptly, and forms one complete loop overlying the large intestine. In Fig. 4 the same thing occurs, but following this first loop are two others. As shown in the figures there is a tendency for the loops to grow around the large intestine from the right side. The large intestine is on the left side of the small intestine and somewhat anterior. The part of the small intestine contained in the cord is less changed, and its growth is apparently somewhat slower. There is, however, to be seen the beginning of a new coil marked *x* in Fig. 4, *B*. This is an incompletely-formed loop and shows well the way in which the loops develop. It is simply a bending, as though the intestine had grown too long for the space it was obliged to occupy. Before reaching the cœcum the small intestine turns on itself in the characteristic way described in Fig. 3. The large intestine is unchanged.

In Fig. 5 the same loops are seen in the first part of the small intestine, and those marked *a*, *b* and *c* correspond fairly well. In the cord, however, there are here too loops instead of the one shown in Fig. 4. These occur in the small

intestine opposite the cœcum and have relatively the same position as the bending of the tube marked *x* in Fig. 4. They are lettered *x* and *y* in Fig. 5. The remainder of the intestine is the same as in Fig. 4. The length of this pig was 25 mm.

Fig. 6 represents the intestine of a pig of approximately the same length as that shown in Fig. 5. The small intestine in the main body-cavity, however, is slightly more advanced in development. The various loops can be readily recognized and much more easily so on the wire model than on the drawing. A very slight change in the general position of a loop causes a most decided difference in a flat drawing. The main difference, for example, between Figs. 5 and 6, is the dislocation of the loop *z* towards the stomach. By comparing the lettering in the two figures this can be easily understood. The part of the intestine in the cord is practically the same in the two figures.

Thus far the large intestine is a simple tube bending sharply near the stomach to form the rectum. It will be noticed that the small intestine has grown much more rapidly than the large intestine; and also that the part of the small intestine near the stomach has increased in length more rapidly than the part in the cord. Several pigs, the same size as these last two described, were examined, and their intestines found to be similar in every way. Embryos taken from the same uterus did not seem to resemble one another in this respect more closely than pigs of the same length from different uteri.

Fig. 7 represents a dissection of a pig's embryo 28 mm. in length, and Fig. 8 is a drawing of the wire model made from this intestine. The stomach, it will be seen, occupies the same position and narrows into the small intestine in the same way as before. The small intestine here forms a distinct mass of loops in the main body-cavity, and then extends out into the cord in a manner identical with that shown in earlier embryos. The loops form a cone-shaped mass with the base of the cone towards the stomach and its apex in the umbilical cord. This is due to the more rapid growth of that part of the small intestine near the stomach. This arrangement will be noticed in all the older embryos as well until after all the coils have returned to the main body-cavity. It is a little unsatisfactory to attempt to follow the individual coils of the intestine, and to trace them from one embryo to another after their arrangement has reached a complexity as great as that shown in Fig. 8 and the figures following. But if the two models represented in Figs. 6 and 8 be compared, there will be seen a certain correspondence which can hardly be overlooked. The identity of the two loops in the cord marked *x* and *y* is recognized at first glance. In this part of the intestine there seems to have been very little if any change. The coils near the stomach, however, are distinctly more complicated in Fig. 8 than in Fig. 6. The slight bend in Fig. 6 marked *e* is accentuated into the loop marked *e* in Fig. 8. The letters *a* and *z* mark corresponding parts in the two figures; and the loop *b* can be readily derived in Fig. 8 from the *b* in Fig. 6. Following this, however, there are in Fig. 8 three distinct loops, *c*, *d* and

f, without counting *x* and *y*; while in Fig. 6 there is only one without considering *x* and *y*. At *d* in Fig. 6 there is the beginning of a new loop, as yet only a slight bending in the tube, and *c* corresponds with one of the three loops spoken of in Fig. 8. There is then in Fig. 6 only one entirely new loop not indicated in Fig. 6.

The cœcum maintains the same position in Fig. 8 as in Fig. 6. The bend in the large intestine, however, where it passes into the rectum, shows quite a distinct alteration. It no longer forms a simple acute angle with the rectum, but is bent in two directions as shown in Fig. 8. This is the beginning of the formation of a very distinct group of convolutions which is perfectly constant and will be described below.

The general tendency in the formation of new loops in the small intestine is for the tube to become slightly bent on itself and to grow around an axis which is represented by the large intestine. The characteristic shape of the loops is shown in Fig. 8, *d* and *f*. The loops do not meet above (on the surface towards the head of the embryo); for the large intestine is situated between the bends of the loops in such a way that it could be lifted away from the small intestine by drawing it towards the head, but not by drawing it towards the tail of the embryo. The arrangement becomes less regular the nearer it is to the stomach, for the growth in this region is more rapid and the pressure exerted on the coils greater than in other parts.

Fig. 9 represents the dissection and Fig. 10 the model of the intestines of a pig 30 mm. long. The general position of the various parts is much like that in Fig. 8. By following the letters on Figs. 8 and 10 the corresponding loops can be made out. There are yet no groups of coils to be distinguished. The small intestine can be roughly compared with a hollow cone whose axis is represented by the large intestine. The loops *x* and *y* have become more fully developed and grow around the large intestine in the characteristic fashion. The loops in the figures are lettered only on the right side, since they are in a certain sense duplicated on the left side of the large intestine. A loop, however, is a fold which begins and ends somewhere in the same neighborhood; and it might be possible to take the median line as the starting point, and make loops on either side; but it is much simpler to treat as complete loops only those folds which start on one side and return to that side.

The large intestine in Fig. 10 holds a straight course from the cœcum until it reaches the stomach. It then makes a complete bend on itself and enters the rectum as shown in Fig. 10, *g*.

Fig. 11 is the dissection of a pig 32 mm. long, and Fig. 12 is a drawing of the model made from its intestinal canal. A certain general resemblance in outline is seen between Figs. 10 and 12. The intestine is a cone-shaped mass in each with the apex extending a short distance into the cord and the large intestine forming an axis for the cone. The arrangement of the small intestine in relation to the large intestine is the same as that spoken of before. The loops

are bent around the axis of the large intestine, especially near the apex of the cone, *i. e.* near the cord. At the stomach end the gut has become so twisted that the individual loops cannot be traced with any satisfaction. Certain landmarks, however, can be recognized. For example, the loops *x*, *y*, *f* and *d* correspond fairly well in the two stages, and it is not difficult to conceive of the transformation of the loop *c* in Fig. 10 to the same loop in Fig. 12. This transformation takes place by a flattening of the loop which will be spoken of later. It gives rise to a figure which is often seen in the intestines of pig's embryos.

Although the loops can no longer be individually followed with ease, there begins at this stage to arise a grouping of the coils. In Fig. 12 four fairly distinct groups can be made out. Starting with the stomach end the intestine forms a mass of loops which are situated mainly on the left side of the body. In no place does a whole coil of this group reach the surface of the intestinal cone on the right side. This will be called group *A*. After bending in five or six loops, as represented in the more lightly shaded part of Fig. 12 near the stomach, the gut reaches the right side and forms a group of more or less flattened coils, which form all the surface coils of the right side up to nearly the beginning of the cord. This group is shaded darkly in Fig. 12 and ends after the loop marked *d*. It includes the coil *c* described above and will be designated group *C*. The intestine leaves this region at the termination of loop *d*, and forms three complete loops of the type described in earlier embryos. These are unshaded in Fig. 12 and include *f*, *x* and *y*. They form the group *D*. These coils are associated more closely than the rest of the intestine with the cœlum of the cord. At the end of this group the small intestine takes a straight path for a short distance and turns on itself in the way seen in all the embryos so far pictured, and enters the large intestine at the cœcum. The large intestine is straight as before until it reaches the region where it turns to form the rectum. Here it is thrown into irregular twists, as shown in Fig. 12, *E*. The convolutions formed in this region will be spoken of as the rectal group or group *E*, and will be followed through the various embryos. At this stage it is directly anterior (towards the head) and lies partly between the groups *A* and *C*.

Fig. 13 represents the model of the intestine of an embryo 40 mm. in length. The general outline of the mass of coils is, as before, cone-shaped. This is accentuated by the increasing complexity of the rectal group, and by the rapidity of growth of the first part of the small intestine. The same groups described above can be recognized at this stage. The group *A* has increased considerably in length in Fig. 13 and can be divided into two groups which are marked *A* and *B* in Fig. 13, *II*. These become more distinct in later stages. From *B* the gut passes over to the right side of the body and forms the group *C* which is situated entirely on the right side, and makes up most of the surface coils there. This is shaded in Fig. 13, *I*. On approaching the cord there are found the three complete loops described in Fig. 12, as making up group *D*. These are almost identical in the two stages, and

extend into the coelomic cavity of the cord, which has become gradually more shallow. The rectal group is more complex than in the preceding stages and forms a conspicuous mass of coils whose calibre is noticeably smaller than in the rest of the intestine. Its position also has altered. Instead of lying between groups *A* and *C*, it is to the right of *C*, having rotated on an axis corresponding approximately with that of the cord.

Figs. 14 and 15 represent the dissection and model respectively of the intestine of an embryo 48 mm. in length. At this stage all the coils are within the main body-cavity. The

large intestine begins on the right side of group *D*, a short distance from its apex. The cœcum corresponds fairly well in position with that in Fig. 13. On leaving the cœcum, however, the large intestine passes obliquely down on the right surface of group *C*, and is coiled to form the rectal group, posterior to groups *A* and *B*. Fig. 14 does not justly represent the regularity of the loops making up group *C*. They form a series lying transversely from right to left, and can be easily separated in a mass from group *D* on the one hand, and groups *A* and *B* on the other.

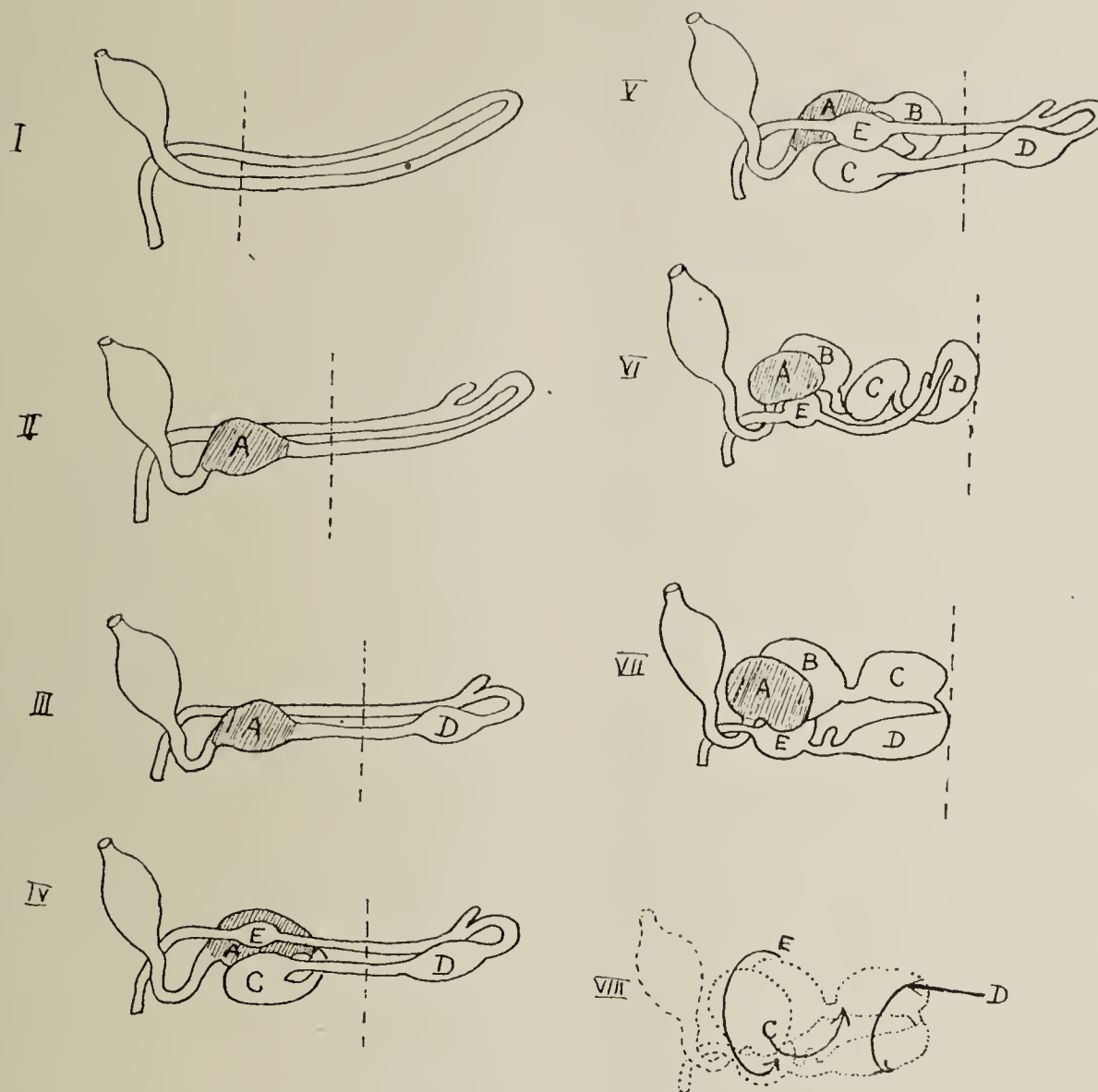


FIG. 18.—A series of diagrams to indicate the formation of groups of coils in the intestine. These represent the intestines of embryos, 12, 21, 25, 32, 40, 48 and 85 mm. in length respectively. The groups are lettered in correspondence with the preceding figures. VIII shows the direction in which the groups have rotated, their course being marked by curved arrows.

groups described above can be readily recognized, but a considerable change in their position has taken place. The surface coils near the stomach are derived from group *A* instead of group *C*, as in the stage represented in Fig. 13. Group *A* is on the right side of the body, and group *B* on the left. Group *C* has moved in a ventral direction and somewhat to the left, until it lies transversely between group *D* and groups *A* and *B*. Group *D* enters the main body-cavity and the regularity of its coils is lost. Instead of being complete and regular, as in Fig. 13, the loops are distorted and flattened by their association with the other abdominal viscera. The more or less pointed extremity of this group is still directed towards the cord, as shown in Fig. 14. The

Fig. 16 represents the surface coils of the intestine of a pig's embryo 85 mm. long. Fig. 16, *I* is drawn from the animal's right side; Fig. 16, *II* from its ventral surface; and Fig. 16, *III* from its left side. The various groups of coils are lettered in correspondence with those pictured in Fig. 17, which is drawn from a wire model of this intestine. The surface coils on the right side are formed by groups *A* and *D*. On the ventral surface groups *B* and *C* are present; while the left side is occupied by parts of *B* and *D* and the whole of group *E*. In this stage the same five main groups, that have been described, can be made out. It will be noticed, however, that their relative position is somewhat different. Group *D* has rotated posteriorly, dorsally and to the right, so

that it takes up a position to the right of, and posterior to, group *C*. It thus moves past group *C* and carries the cœcum with it, so that the beginning of the large intestine lies dorsally, and posterior to group *D*. The group *E* is pushed still farther in the same direction until it is finally situated in the left dorsal region of the mass of intestines. This group in the beginning lies on the left anteroventral surface. As it becomes more complex it moves around to the right until it reaches the left dorsal position. It therefore rotates through three-quarters of a circle. The axis of this rotation is a line drawn from the beginning of the duodenum to a point somewhat posterior to the umbilical cord.

Fig. 18 consists of a number of diagrams of the different stages, showing this rotation of the groups. The straight dotted line in each diagram represents the junction of the main body-cavity and the cœlom of the cord. Diagram VI corresponds with Fig. 15, and VII with Fig. 17. The younger stages can be easily recognized. Diagram VIII shows the direction in which the groups rotate. The letters in all the diagrams correspond with those used in the description of the groups; and in VIII these letters, associated with the curved arrows, indicate the direction in which those groups have moved from their original positions.

An appearance which is characteristic of the older embryos is shown in Fig. 16, *I*, *D* and *C*; and in Fig. 16, *II*, *C*. The regular loops, which have been described, become flattened by pressure against the abdominal walls, giving rise to the peculiar coiled appearance represented.

The intestines of several embryos older than those represented in Figs. 16 and 17 were studied. The groups were found to correspond with those already described; and an account of these later embryos would not add any essentials to the above description. It is possible in these to tell with considerable accuracy to what group any one surface loop belongs.

It will be noticed that in the older stages, which have been described, the large intestine grows more rapidly than it does in earlier embryos. In those represented by the first eight figures there is practically no change in the large intestine. After this, however, there gradually appears a considerable mass of coils to form the rectal group. The part of the small intestine which is at first present in the cord grows more rapidly after its return to the general body-cavity. For this reason as well as on account of the pressure exerted by the other viscera, the cone-shaped mass of intestines becomes more or less spherical after it is entirely intra-abdominal. The growth, which in earlier stages was almost solely in the region of group *A*, is in the older embryos more uniform throughout the gut. The younger the embryo, the more noticeable is this rapid growth in the region of group *A*. This fact was observed by Dr. Mall and indicated in his paper by means of tables of measurements. In connection with this it is of interest to note an observation made by Berry,⁶ who found that the villi appear first in the upper part of the

intestine. Whether or not the number of villi increases more rapidly in this region than lower down, has not been determined.

In reviewing a considerable number of embryos in this way and modeling their intestines by a method in which errors can be easily controlled, one cannot help being struck by the remarkable constancy of the appearances met with. At first glance it is more noticeable in the earlier embryos. This fact is due to the greater simplicity of the loops and to the smaller chance for distortion of the coils by pressure. It will be noticed that there is practically no variation in the portion of the intestine contained within the cord. In that part of the body-cavity there are no other viscera to interfere by pressure with the growth. If it were possible to isolate an organ during its development, its form would undoubtedly be different from what it is when it develops a contact with many other growing organs. The portion of the intestine which develops in the cord is to a certain extent isolated. The rapidly-growing viscera, such as the liver and urinary organs, can in no way interfere with its growth; and it is seen from the above descriptions that it is this part of the intestine in particular, which is entirely constant in its appearance. Here the intestine increases in length by the formation of regular loops which grow up and surround the large intestine, as already stated. At first sight it would appear that this manner of growth might be caused by the confinement of the intestine in the cylindrical cavity of the cord; but the same method of formation of loops takes place in the general body-cavity before any loops whatever appear in the intestine of the cord. Since it thus takes place in two parts of the intestine under different conditions, it is fair to assume that this is the natural tendency in the growth of loops in the intestine of the pig.

Dr. Mall, in the publication already referred to, has discussed the entry of the intestinal loops into the cœlom of the cord, and their return to the general body-cavity. He inclines to the belief that the gut is forced into the cord by the pressure exerted on it by the other rapidly-growing viscera; and that it returns to the main body-cavity on account of a twisting of the loops already contained in the abdomen. The dissections of the pig's embryos, which have been described, throw no new light on this subject. The cœlom of the cord in early pig's embryos is of considerable size and the intestine is at first only a single loop. Hence it is not hard to imagine its being pushed into this easily available space in the cord. Here it remains until the secondary loops are formed, which make up group *D*. This group is more or less cone-shaped and fits into the cavity of the cord which has a similar form. The passing of this group to the main body-cavity does not take place one loop at a time. The group returns apparently by a gradual obliteration of the cone-shaped cavity of the cord from its apex to its base.

It can hardly be said that the coils enter the abdominal cavity from the cord in any regular order. The order of their entry is dependent on their position in the mass of coils which projects into the cord. The apex of this mass is formed by

⁶ Berry, J. M.; Anatomischer Anzeiger, xvii Bd., S. 242, 1900.

the lower end of the ileum where it turns on itself to join the large intestine. The apex leaves the cord last, and hence the lower end of the ileum is the last part to enter the abdominal cavity. In the same way the cœcum enters a short distance in front of this part of the ileum, simply because it is so situated in the group of coils.

In connection with the development of the mammalian intestine, I wish to call attention very briefly to the intestines of the various lower vertebrates. In *Amphioxus* the alimentary canal consists of a simple straight tube with no convolutions whatever (Fig. 19, *A*). In the shark the intestine is straight, but the stomach is bent on itself so as to form a descending, and an ascending part (Fig. 19, *B*). In the perch, as in most Teleosteans, there is one distinct loop in

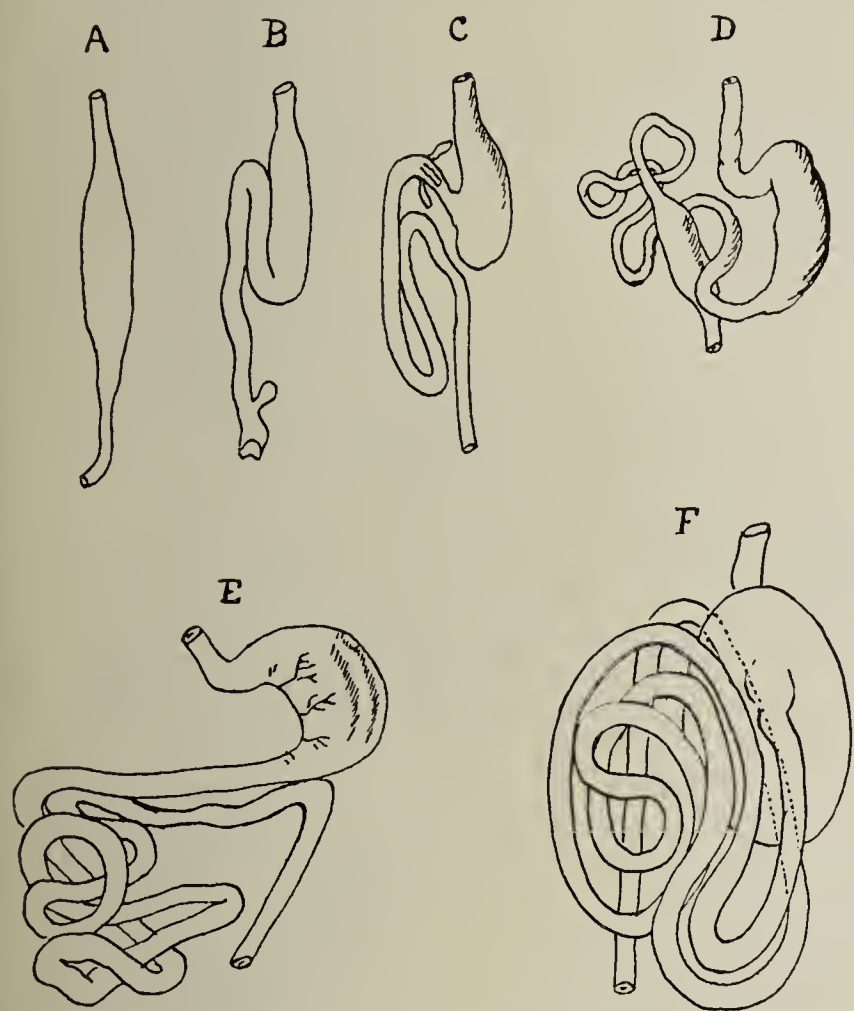


FIG. 19.—Diagrams representing the intestines of *A*, *Amphioxus*; *B*, Shark; *C*, Perch; *D*, Frog; *E*, Turtle; *F*, Sparrow.

the intestine, as shown in Fig. 19, *C*. There are two methods in these animals by which the digestive surface is increased in extent, namely, by the so-called spiral valve and by the pyloric cœca. The spiral valve consists of a longitudinal fold extending into the cavity of the intestine. It is present in all Elasmobranchs, Dipnoi and Ganoidei, but not usually in the Teleostei. The pyloric cœca may be very numerous and form a large mass of processes just below the stomach. The spiral valve and the pyloric cœca are seldom both highly developed in the same animal.

In the Amphibia the intestine is, as a rule, much more complex than in the fishes. As shown in Fig. 19, *D*, the frog's intestine is considerably coiled. In a number of frogs and toads which were dissected, the intestines were found to be arranged according to a general type which is represented

in Fig. 19, *D*. In some cases, however, the coils assumed a much more complicated mass than that shown in the figure. It is interesting to note here that in some stages of the tadpole's life the intestine is a much more complex organ than in the adult frog. The intestine of *Necturus* shows a coiling which is usually not so great as in the frog.

In the Reptilia the form of the alimentary canal is considerably modified by the shape of the body. In Fig. 19, *E*, is represented the stomach and intestine of a turtle. This is an arrangement which was found to be very constant. In snakes the coils are not so numerous and are somewhat obliterated by the narrowness of the body. In lizards the intestine is coiled more than in either the turtle or the snake. Thus it is seen that in reptiles, and amphibians there is a much more complex arrangement of the coils of intestines than in fishes.

In birds there is a still greater complexity in the form of the intestine. Birds of the same species show very little variation in the arrangement of the coils. In a number of sparrows, robins and blackbirds the arrangement was found to be according to a type represented in Fig. 19, *F*. There was very little divergence from this type in any of the specimens examined. In the chicken, however, there is a far greater coiling. In several chickens examined there was found a noticeable constancy in the arrangement of the loops. A long duodenal fold extends from the gizzard backward and to the left side of the body. Turning on itself it passes to the right side of the body, where the small intestine is thrown into a number of coils which resolve themselves into two main groups. From the rectum two long cœca extend forward.

In the study of these few lower vertebrates two main points are to be observed: (1) the constancy in the arrangement of the loops in nearly related animals; and (2) the gradual increase in complexity of the coils as we pass from the lowest vertebrates to those higher up in the scale. It is interesting to note also a certain relation which seems to exist between the ontogeny of the intestinal canal in mammals, and its phylogeny. Beginning with a straight tube in the early mammalian embryo the intestine is thrown into a gradually increasing number of loops. Beginning in the same way with *Amphioxus* we may pass from the fishes, which possess but a single loop, to the amphibians, whose intestine is much more complex; and from these to the birds and mammals, where the alimentary canal is a very much coiled organ.

RECAPITULATION.

The intestine of a pig's embryo at an early stage consists of an uncoiled tube which sends a single loop out into the coelom of the cord. The first half of the loop is on the right side and gives rise to the small intestine. From the other half is formed the large intestine. The gut increases in length by the formation of regular loops which grow around an axis corresponding with that of the cord and the large intestine. These loops form first in the part which is to become the small intestine. They also develop in that part of the small intestine near the stomach before they appear in

the cord. Up to a certain stage the further growth in complexity is greatest near the stomach. After the small intestine has become considerably coiled, a mass of loops is formed in the large intestine. In embryos between 35 mm. and 40 mm. in length the group of coils which has formed in the coelom of the cord, enters the general body-cavity by a mechanism which is not clearly understood. In embryos of the same size the coils are constant in arrangement and definite in their position. They can be followed through various stages of the early development. In older embryos, when the individual coils cannot be recognized with ease, they are found to be arranged in distinct groups which have definite situations in the body-cavity. The loops in a certain region of the body-cavity, though they may vary in form, always belong to the same group. These groups arrive at their final situation by a rotation which takes place posteriorly and to the right around an axis, running from the beginning of the duodenum to a point a short distance posterior to the opening of the cord. It is not at all claimed that the surface coils hold always the same position with regard to one another, or that the coils always have the same relation to one another in the group; but it is to be emphasized that the groups always do hold the same relative position in the body.

In lower vertebrates the intestine increases in complexity as we ascend the scale. The intestinal coils are very similar in nearly related animals; and a certain amount of constancy is noticed in their arrangement.

I regret that I have had no opportunity of confirming Dexter's work on the cat's intestine, in which he finds no constancy in the position of the loops. However, from the researches, already referred to, of Henke, Weinberg, Mall and Merkel, as well as from the present study of pig's embryos and the intestines of lower vertebrates, it seems plain that the intestinal canal is an organ which is situated in the body in a definite position, and that its different parts hold a constant relation to one another.

DESCRIPTION OF PLATES XIX-XX.

FIG. 1.—Pig's embryo 12 mm. long, showing a single loop of intestine extending into the umbilical cord.

FIG. 2.—Pig's embryo 18 mm. long, showing a loop of intestine in the cord with a distinct coenm. The small intestine shows the beginning of coils inside the main body-cavity. The dotted line indicates the original outlines of the body before the removal of the liver.

FIG. 3.—Pig's embryo 21 mm. long, showing a slightly more convoluted small intestine. The numbers 1, 2 and 3 correspond with those on Fig. 3.

FIG. 4.—A. Dissection of pig's embryo 23 mm. in length.

B. Wire model of the intestine of this embryo.

FIG. 5.—Wire model of intestine of pig's embryo 25 mm. long. The lettering corresponds with that in Fig. 4, B.

FIG. 6.—Wire model of intestine of pig's embryo 25 mm. long.

FIG. 7.—Dissection of pig's embryo 28 mm. long.

FIG. 8.—Wire model of intestine of the embryo represented in Fig. 7.

FIG. 9.—Dissection of a pig's embryo 30 mm. long.

FIG. 10.—Wire model of intestine of embryo represented in Fig. 9.

FIG. 11.—Dissection of a pig's embryo 32 mm. long. C, superficial group of coils on right side of body. The small letters correspond with those used above.

FIG. 12.—Wire model made from the intestines of the embryo represented in Fig. 11. A, C, D and E, indicate the formation of groups of coils. The group C is shaded.

FIG. 13.—Wire model of intestine of an embryo 40 mm. in length. The groups are lettered as in Fig. 12.

FIG. 14.—Dissection of a pig's embryo 48 mm. long. The letters as before indicate the groups of coils.

FIG. 15.—Wire model of intestines of embryo represented in Fig. 14. Groups are indicated by shading.

FIG. 16.—Dissection of a pig's embryo 85 mm. long. I shows the intestines from the right side; II from the ventral surface; and III from the left side. The lettering corresponds with that in the previous figures.

FIG. 17.—Wire model of intestine of embryo represented in Fig. 16.

NOTE:—No attempt has been made to retain the relative size of the embryos in these figures. The actual measurements are given in each case.

BILATERAL RELATIONS OF THE CEREBRAL CORTEX.

BY E. LINDON MELLUS, M.D.

(From the Anatomical Laboratory, Johns Hopkins University.)

In the study of the central nervous system it becomes more and more apparent that the statement that each cerebral hemisphere controls the opposite half of the body must be still further modified. It has long been recognized that certain movements were more or less bilateral; that is, equally controlled by each hemisphere. This is easily demonstrated by electrical stimulation of the cortex and, to a certain extent, the anatomical relations have been worked out. The bilateral representation of most facial movements would appear at first thought to be quite essential and anatomists held, long before it was demonstrated, that each of the motor nuclei in the pons and medulla was connected with its fellow of the opposite side by decussating fibres. Bilateral movement

could thus be accounted for by simultaneous stimulation of the nuclei of both sides, but the results of some of the more recent investigations show that projection fibres run directly from the cortex of each hemisphere to the nuclei of both sides. This provides for simultaneous stimulation, while the fibres passing directly from one nucleus to the other may conserve the symmetrical discharge of energy.

The necessity for bilateral control of the limbs is not so evident, but the fibres of the so-called direct or uncrossed pyramidal tract in man and the finding of bilateral degeneration in the cord after unilateral lesion of the brain seemed to make it probable. For some time it was not possible to trace the course of this homolateral degeneration from the



FIG. 1.



A

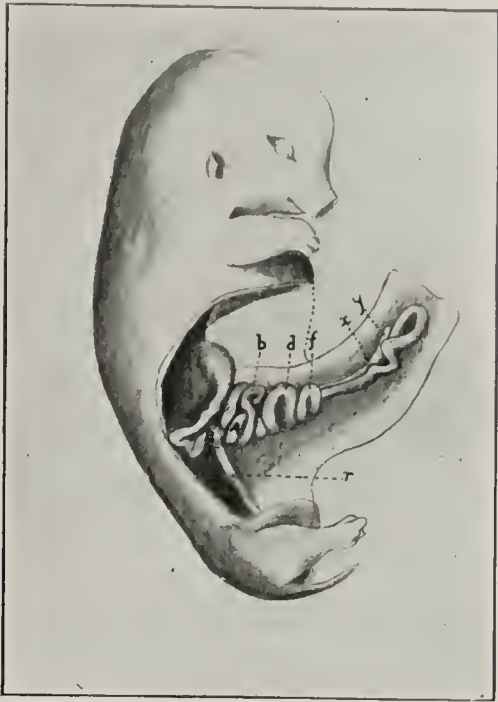


FIG. 7.



FIG. 2.

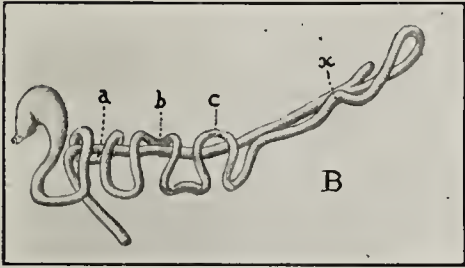


FIG. 4.

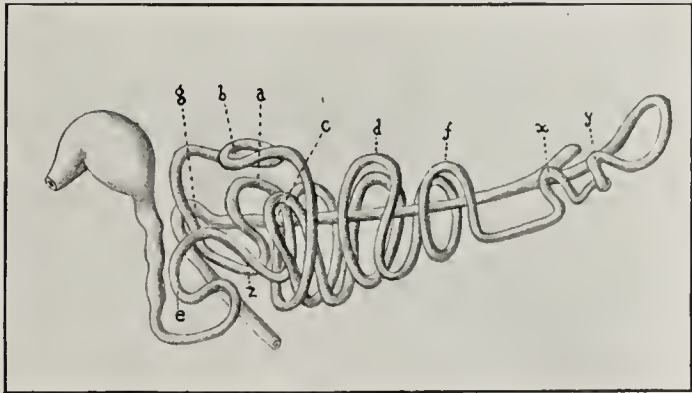


FIG. 8.



FIG. 3.

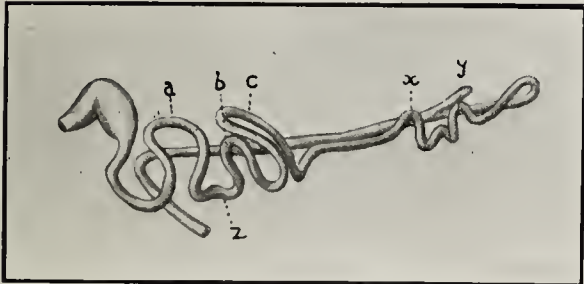


FIG. 5.



FIG. 9.

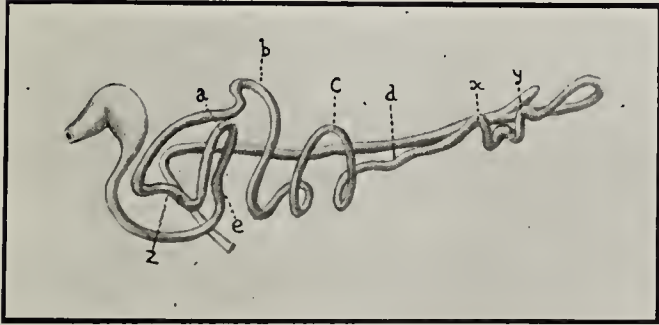


FIG. 6.

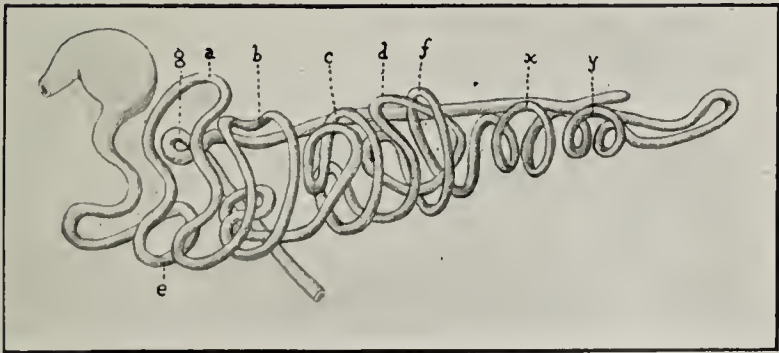


FIG. 10.

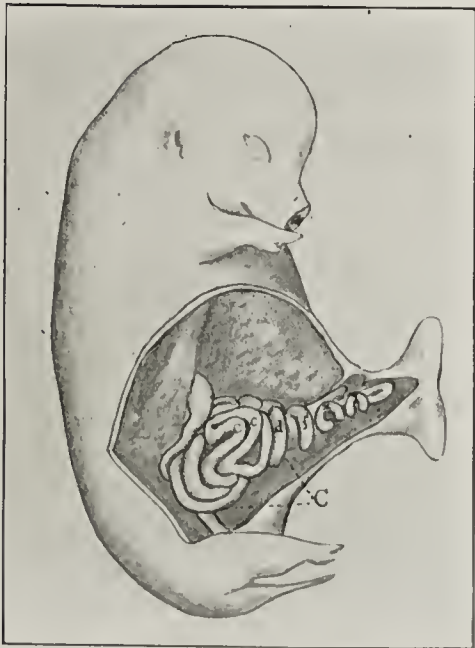


FIG. 11.

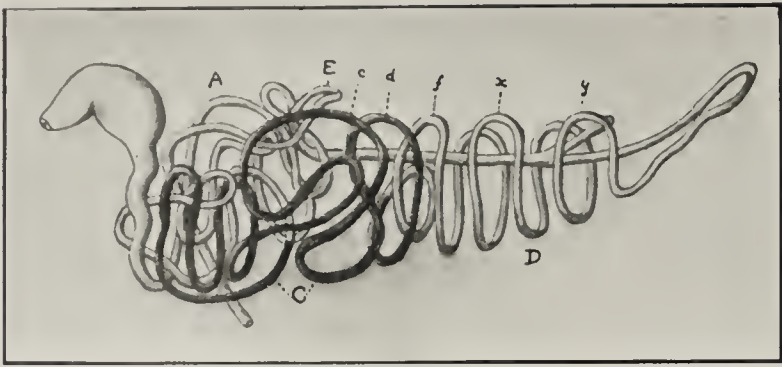


FIG. 12.

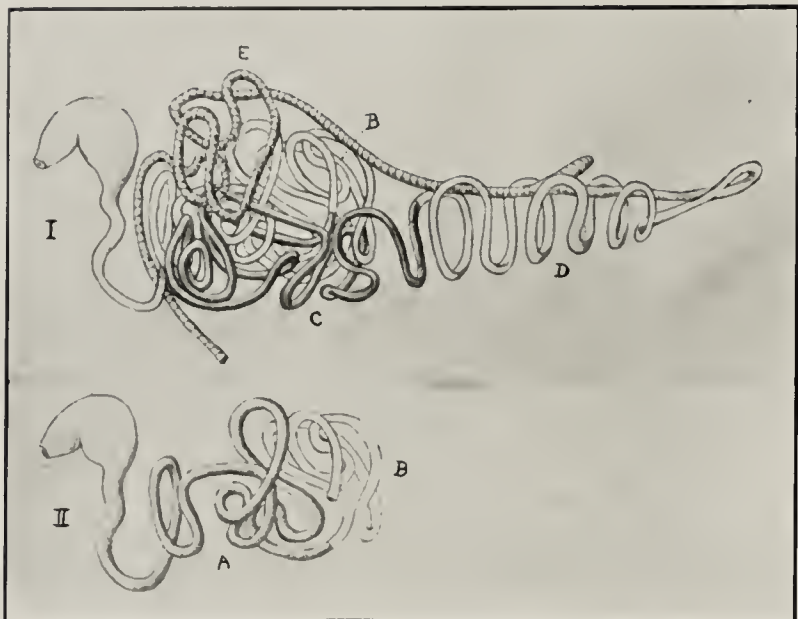


FIG. 13.

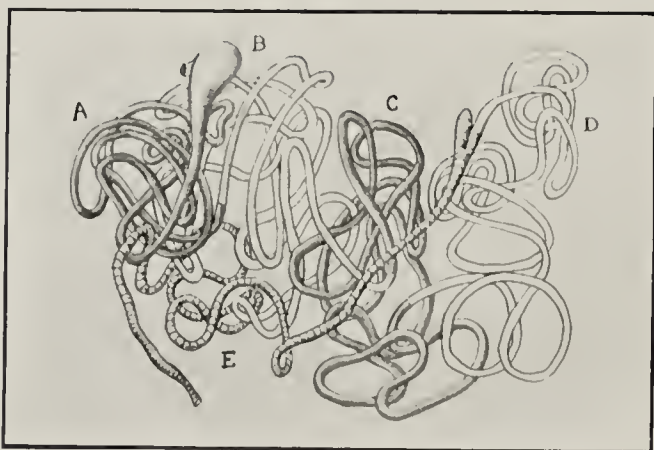


FIG. 15.

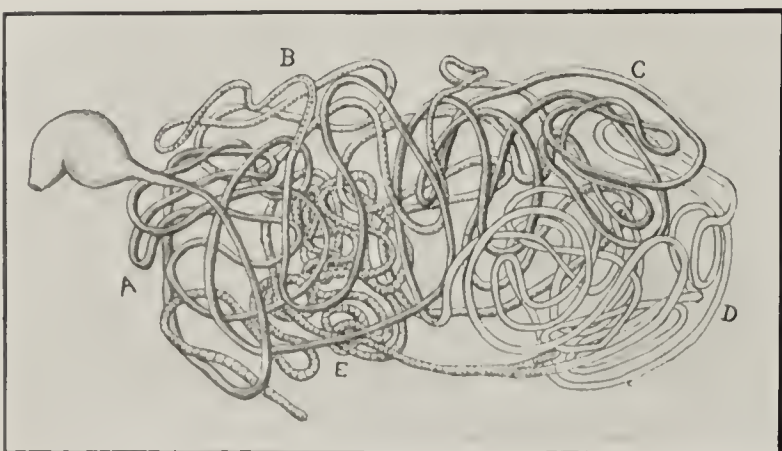


FIG. 17.

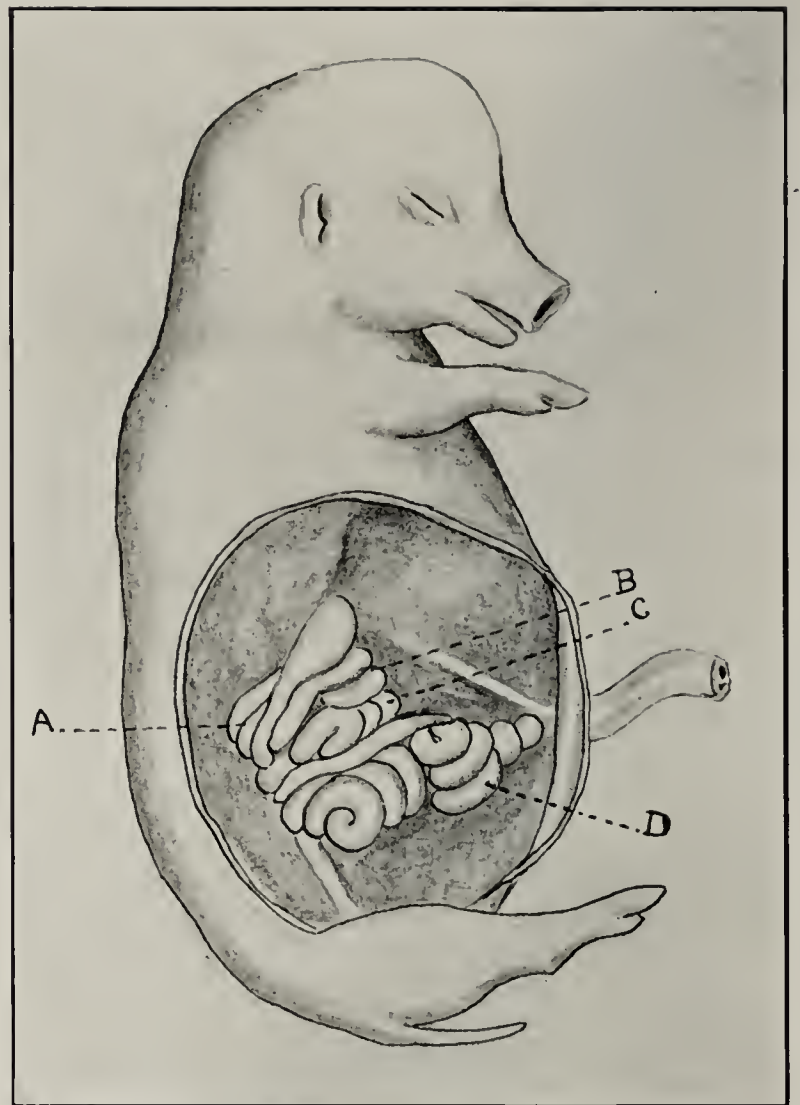


FIG. 14.

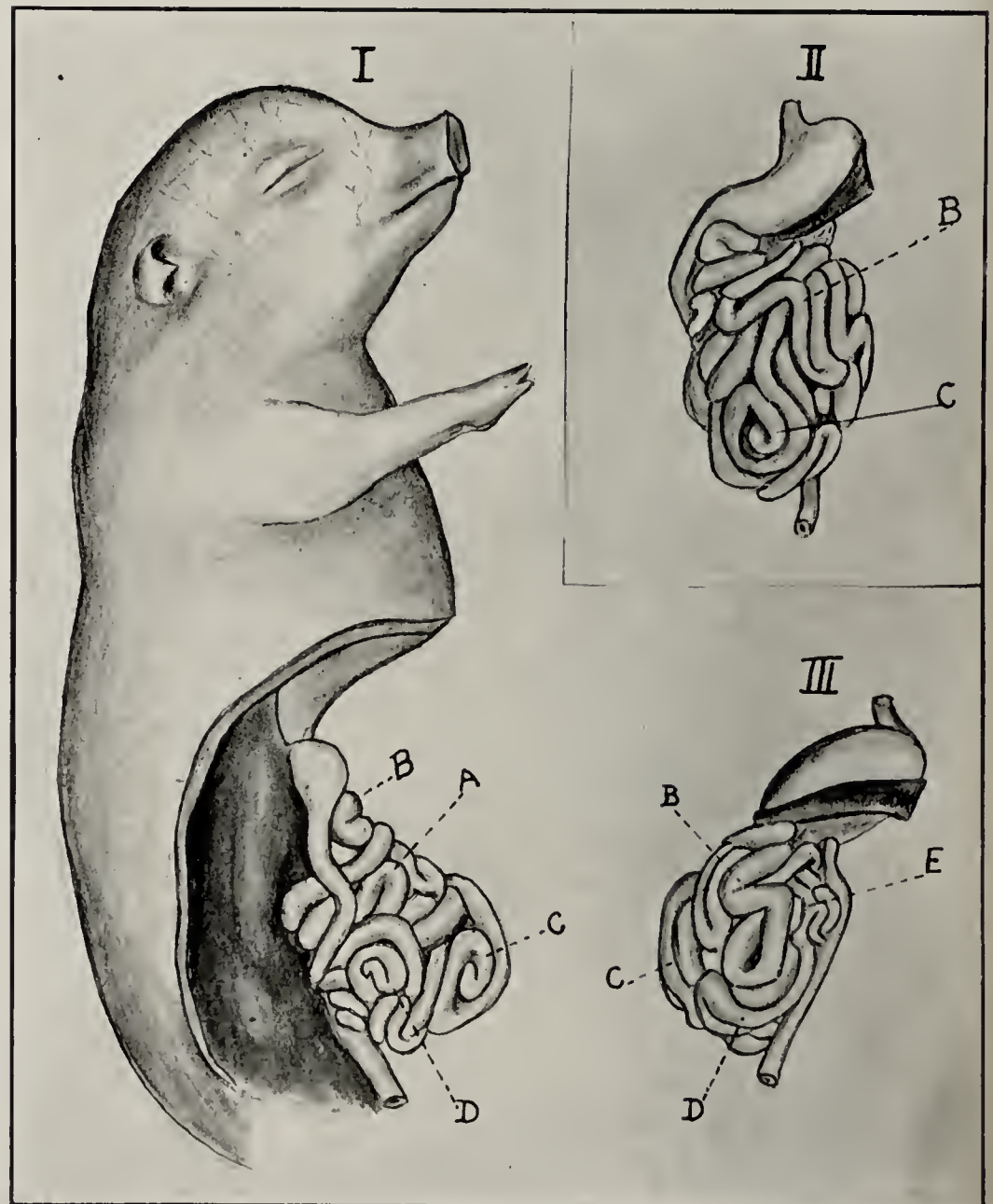


FIG. 16.

brain to the cord, and various theories were brought forward to explain it. It was considered probable by some anatomists that the pyramidal tract divided at the decussation, some fibres passing to the lateral column of each side, while a portion remained in the anterior column as the direct tract; but in the absence of confirmation Sherrington's theory of "recrossed" fibres was generally accepted. Sherrington's conclusions were based upon experimental unilateral lesions on the brain of the monkey, in which he claimed that immediately below the decussation the degeneration was all on the opposite side of the cord, while at a still lower level degenerated fibres were found in both lateral columns. He thereupon assumed that all the degeneration crossed over in the decussation to the opposite side of the cord, but a portion crossed back at a lower level to the lateral column of the same side. The probable explanation of his mistake is that at the time of his observations the delicate methods in use in recent years were not known. Still the fact that he reported at the same time that fibres from the upper limb area of the cortex passed down the entire length of the cord, while fibres from the leg areas disappeared from the cord in the cervical and upper dorsal regions, would indicate that his preparations were handled or studied somewhat carelessly. It is rather curious that no one seems to have suggested that he had mixed up those cords.

Soon after the publication of Marchi's method of staining degenerated nervous tissue by osmic acid, Muratow undertook the study, by that method, of degenerations following lesions of the brain in the dog. He published the results of his observations in 1893¹ and clearly showed that in the dog the pyramidal tract divided at the decussation and a portion passed directly to the lateral column of the same side. I had been working with the same method tracing degenerations in the central nervous system of the monkey after very minute lesions of the cerebral cortex, and at the time of the appearance of Muratow's publication I had already accomplished the same results on the monkey, but to him undoubtedly belongs the credit of priority. These results have since been confirmed by other investigators, and Dejerine and Thomas² and Risien Russell³ have proved the existence of the same conditions in man.

At the same time I was able to demonstrate the passage of fibres from the pyramid of one side directly to the motor nuclei of both sides in the pons and medulla.⁴

The following experiment enlarges still further the scope of bilateral representation and adds another to those paths already demonstrated by which one hemisphere may control more or less both halves of the body. It by no means stands alone, but is presented as the type of a considerable group which will be considered individually in a later publication.

On September 20, 1898, I operated in Mr. Victor Hors

ley's laboratory at University College, London, on a small but apparently healthy bonnet monkey (*Macacus sinicus*). The animal being etherized, the cortex of the left hemisphere was exposed under strict aseptic precautions, the centre for thumb movements determined by electrical stimulation and that portion of the cortex carefully excised. Care was taken not so much to remove every portion of cortical substance as to avoid injury to the underlying white matter. I therefore passed the knife under the cortex with the flat surface of the knife parallel to the convexity of the hemisphere, bringing it out at a right angle to the line of incision. Then lifting the cut edge with a pair of small forceps the excision was easily completed. The slight hemorrhage was controlled with hot saline solution, the wound closed with horsehair sutures and dressed with borated cotton smeared with colloidion. This monkey got diarrhoea and died on the tenth day after the operation (September 30) of marasmus. The wound in the scalp had healed well and there was no trace of sepsis. The brain and cord were removed, kept for four days in formalin and then transferred to Müller. The brain was cut into thin segments in a plane nearly parallel to the occipital sulcus (*Affenspalte*), as shown in Figs. 1 and 2, and stained by the Marchi method. It was my endeavor to make the plane of section correspond as nearly as possible to the course of the projection fibres through the internal capsule.

DESCRIPTION OF THE LESION.

The portion of cortex removed was circular and about one cm. in diameter. About one-third of the area of the lesion was in the ascending parietal convolution and the other two-thirds in the ascending frontal. Its posterior extremity was about midway between the lowest portion of the interparietal sulcus and the fissure of Rolando, while its anterior boundary was the superior angle of the sulcus precentralis. The lowest portion of the lesion was very nearly opposite the lower extremity of the interparietal sulcus, and it extended upward to the superior frontal sulcus.^{4a} The lesion in the ascending frontal was much more shallow than in the ascending parietal and the entire cortical substance was removed only at that portion of the ascending parietal convolution nearest the centre of the lesion, close to the fissure of Rolando. It was at this point that uncomplicated flexion of the thumb was obtained on stimulation with a weak faradic current. The portion of cortex removed became thinner from the centre to the periphery of the lesion. In the hardened brain there was evidence of slight cerebral hernia, *i. e.* bulging of the brain into the opening in the skull, which accounts for the irregularity of contour in Fig. 3.

In Figs. 1 and 2 I have endeavored to show the distribution of association fibres to the external surface of the two hemispheres, the proximity of the oblique parallel lines to each other corresponding to the amount of degeneration found in the various convolutions. It was impossible to

¹ Archiv für Anatomie und Entwicklungsgeschichte. 1893.

² Dejerine and Thomas. Archives. de physiol. norm. et patholog. 1896, No. 2. Review in Neurologisches Centralblatt, 1897, p. 503.

³ Risien Russell. Brain. Summer, 1898.

⁴ Proc. Roy. Soc. vol. 58.

^{4a} In Fig. 1 the lesion does not extend upward as far as it should. It is better represented in Fig. 3.

represent the comparative amount of degeneration so accurately in the outline drawings of transverse sections of the brain (Figs. 3 to 7 inclusive), because in so small a figure, in order to have the degeneration show at all, it was necessary to exaggerate. Degenerated fibres can be seen crossing in the corpus callosum in all the segments except "E," the most posterior. The distribution of association fibres to the convolutions of the two hemispheres is very nearly equal and quite symmetrical. It extends also upon the internal (mesial)

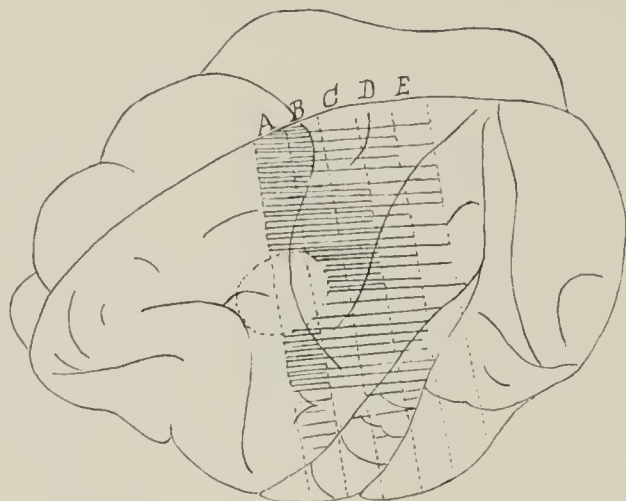


FIG. 1.

surface of both hemispheres as far as the calloso-marginal fissure.

In two segments, C and D, the degeneration extends to the superior temporal convolution of both sides. The route taken by the degenerated fibres to reach the temporal lobe is the same in both hemispheres and is interesting. In section "B" (Fig. 4) a few degenerated fibres appear among the fibres passing to the superior temporal convolution just external to the thickened lower edge of the claustrum on both

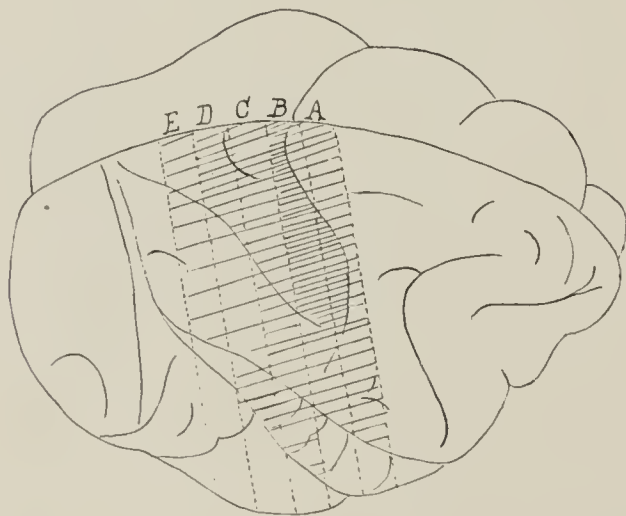


FIG. 2.

sides. In the segment posterior to this (Fig. 5) many degenerated fibres can be seen leaving the internal capsule, breaking through the thin inferior edge of the lenticular nucleus and passing below the claustrum to reach the superior temporal convolution. Some of these fibres probably terminate in the lateral geniculate body. Although no continuous fibres could be traced from the internal capsule into the lateral geniculate body, it lies directly in the path of those running to the temporal lobe and there is considerable degeneration

in this nucleus in both hemispheres. Still posterior to this (Fig. 6) degenerated fibres are passing between the islets of gray matter representing the prolongations of the putamen, while many others may be seen passing down among the fibres of the external capsule. The degenerated fibres in the superior temporal convolution are apparently continuous with both these tracts, the course of which is the same in both hemispheres.

Taking into consideration the movements represented in

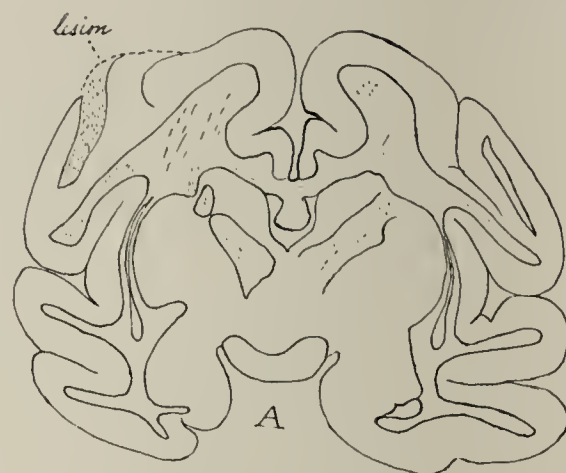


FIG. 3.

that portion of the cortex removed, the distribution of association fibres is of especial interest. While the centre for *uncomplicated* movement of the thumb occupies but a small portion of the area removed, movements of the thumb as part of some associated movement or march may be obtained not only from every portion of that area but also from points considerably removed therefrom—even as far down the convexity of the brain as the lower extremity of the fissure of Rolando. It is a question of much interest whether this is



FIG. 4.

brought about by means of association fibres or projection fibres passing directly from each of the widely separated cortical areas to the system of secondary neurons in the cervical region of the cord. It is quite possible that complicated movements may be brought about in either or both ways. The great increase in cortical association tracts between monkey and man suggests the possibility of inconceivable degrees of association.

Looking upon the motor cortex as representing the centres

for associated movements one would naturally expect to find projection fibres passing directly down through the capsule from that part of the cortex, giving rise to the movement. As I understand the significance of excitation experiments upon the cortex, the finding of a centre for the uncomplicated movement of the thumb only means that in the movement represented at that spot, the movement of the thumb (flexion or otherwise) is the first or initial movement of the march. If the stimulation is continued or increased the

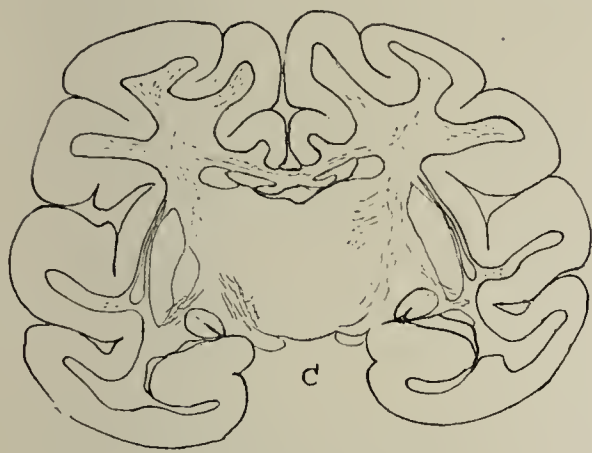


FIG. 5.

march is continued or completed unless interrupted by a general convulsion. Thus, if the anaesthesia is at just the right stage the gentlest stimulus only excites the first or initiatory movement of the march. In opposition to such a theory it may be urged that only one centre has been found in any single animal for such uncomplicated or initial movement, while many combinations are possible beginning with such movement. This would hardly render an entirely separate centre for each movement necessary, as they might all be grouped about the common centre.

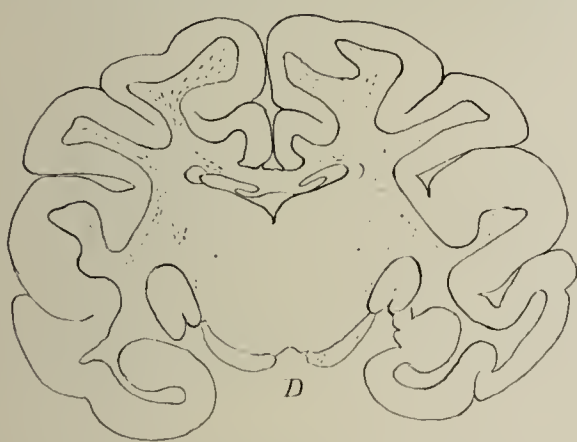


FIG. 6.

In experimental destruction of small cortical areas in the monkey I have often traced projection fibres into the cervical region of the cord from portions of the facial area far removed from arm centres. Such fibres probably represent the conduction paths for impulses, giving rise to movements in which the arm is associated with facial movement. Such movements or actions are numerous in the monkey and increase as we go up in the scale. For example, in feeding, the monkey stretches out his arm, opens the hand to lay hold

of the object, which he grasps and carries toward his already opening mouth. In this instance the extension of the arm is the initial movement, followed by extension of the thumb and fingers, then flexion, etc. Such a movement or march is of course much more complicated than any movement obtained by electrical stimulation of the cortex. But it must be assumed that the normal discharge of energy from the cells concerned in the cortical reflex, as a result of incoming sensations, is a very different affair from our experimental stimulation. Stimulation of the motor cortex with a weak faradic current gives rise to certain movements. Cut away the cortical cells and stimulate the cut ends of the projection fibres immediately beneath and you get the same result. Who can say these results are or are not brought about in the same way? Does the former experiment induce a discharge of energy from the cell or does the current passing through the cell to the axis cylinder act exactly as in the other instance? However this may be we cannot safely assume that stimulation experiments disclose more than a hint of the functional activity of the cortex.

A study of the excitation experiments of Beevor and Horsley⁵ on the bonnet monkey shows that they obtained from

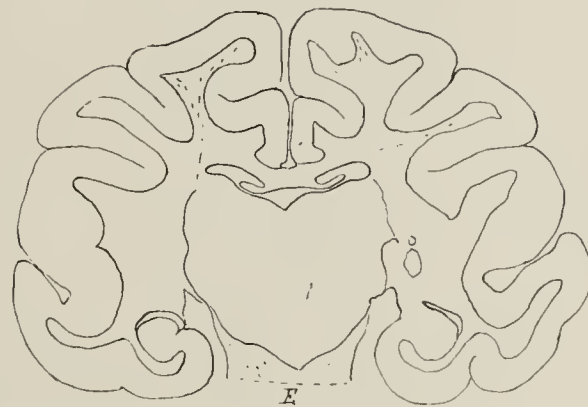


FIG. 7.

the cortical area corresponding to the lesion in this experiment:

Movements of thumb of the opposite side; flexion, extension and adduction;

Flexion and extension of the fingers, opposite side;

Movements of wrist, elbow and shoulder, opposite side;

Closure of opposite eyelids;

Turning of the head to the opposite side;

Retraction and elevation of the corner of the mouth, opposite side;

Pouting, pursing and rolling in of the lips, more of the opposite side, but often bilateral;

Opening of both eyes and

Retraction of the head.

The last two were each observed only once in fifteen experiments. These movements were obtained from various points within the given area but in no single animal were they all observed, nor was any one of these movements obtained from exactly the same point in all the animals experimented upon. Most were primary, though sometimes secondary or tertiary.

⁵ Beevor and Horsley, Phil. Trans. Royal Society, B. 1887 and 1894.

No purely primary movement was observed of the elbow or the fingers.

On stimulation of the cortex of the orang outang the same investigators⁶ observed opening of the eyes and turning the head and eyes to the opposite side represented in the same area, or rather in that part of it anterior to the fissure of Rolando. This march, it will be seen, is also represented within this area in the Bonnet, though not so clearly brought out as in the latter. It is of especial interest in connection with the considerable degree of degeneration found, in the experiment here described, in the superior temporal convolution, now well established as the auditory centre. The association of this centre with that portion of the cortical area which controls the opening of the eyes followed by synchronous movement of the head and eyes would seem to be the anatomical basis of a cortical reflex of primary importance to self-preservation in all wild animals. It is also to be noted that the distribution of these fibres is quite bilateral. The fact that in this case they degenerate toward the auditory centre, instead of from it, may be urged against the supposition that these fibres are a link in this reflex, but the anatomical relations of the two centres are certainly intimate and direct.

The feature of special interest in this group of experiments is the large number of degenerate fibres passing from the area of the cortical lesion over the middle line in the corpus callosum and down the internal capsule of the opposite side.⁷ With the exception of those fibres going to the superior temporal convolution of the opposite side, these fibres, in this experiment, all pass into the thalamus. In a few animals, in which practically the same area was extirpated, some of the degenerated fibres found in the internal capsule of the opposite side can be followed through the pons and medulla into the cervical region of the cord where they disappear.

Nerve fibres within the central nervous system usually functionate in the direction of degeneration, but there is nothing in the character of the degeneration to suggest the character of the function. This can only be guessed at by the origin, course and termination of the fibres and what

⁶ Beevor and Horsley, Phil. Trans. Royal Society, B. 1890.

⁷ The writer has found the same thing—degeneration in the internal capsule of both sides after unilateral lesion in the brain, in the dog. In the dog all the degeneration in the internal capsule of the opposite side ends in the thalamus.

we know of the function of the areas and structures thus anatomically associated. Some of the projection fibres passing inward from the motor cortex clearly carry motor impulses, but it cannot be assumed that all do. A vast number of projection fibres arising in the motor cortex end in the thalamus; I think I may say in the thalamus of both sides. A careful study of the brains of a large number of animals, mostly monkeys, the subjects of experimental lesions of the cortex, leads me to conclude that this anatomical connection of each thalamus with the cortex of both hemispheres is most evident in those instances in which the area excised was that in which movements more or less bilateral are represented. These movements are mostly facial; such as are called into play in the expression of the emotions. May not this have some bearing on the function of the thalamus? It has been suggested that the thalamus is the centre for reflex or emotional movements.⁸ In unilateral facial palsy the escape of the emotional paths has long been a puzzle. According to present conceptions the cortex is concerned in all reflexes involving consciousness. Many cortical reflexes are purely voluntary. The part played by volition in those cortical reflexes termed emotional, such as the play of the features in facial expression, is open to discussion, but it can hardly be doubted that they are as much cortical reflexes as any of the so-called voluntary movements. The interposition of the thalamus in such an arc and the anatomical connection of each hemisphere with both thalami, as here demonstrated, may explain the play of the features as the result of emotion when voluntary movement is impossible. In many extensive lesions of the internal capsule fibres passing into the thalamus, even on the side of the lesion, might easily escape injury, even if bilateral control of the thalami were improbable.

As to the functions, other than motor, of projection fibres from the motor cortex, it is at least possible that some serve the purposes of inhibition, voluntary or otherwise. It seems altogether reasonable that voluntary inhibition of certain visual reflexes might be essential to holding the eyes fixed upon a given object. This is suggested as a possible explanation of the presence of degenerated fibres in the lateral geniculate bodies in this case (Figs. 5 and 6). There is certainly no reason why the reflex might not be inhibited in the geniculate body before it reaches the motor oculi nuclei.

⁸ Beehterew. Leitungsbahnen im Gehirn und Rückenmark. Zweite Auflage.

A NEW CARBON-DIOXIDE FREEZING MICROTOME.

BY CHARLES RUSSELL BARDEEN, M. D.,

Associate in Anatomy, The Johns Hopkins University, Baltimore.

The carbon-dioxide freezing microtomes in common use in pathological laboratories have several drawbacks. Of these the most serious are those due to the use of a rubber tube to connect the tank with the freezing stage. In addition to the

annoyances due to the rubber tube the microtomes are so constructed as to utilize but a slight fraction of the heat absorption due to the expansion of the liquid carbon-dioxide. In order to obviate these drawbacks the microtome described

below was devised. In the designing of the original machine I had the assistance of Mr. E. F. Northrup. In the construction of the present machine I am indebted to Bausch and Lomb, who manufacture it, for several modifications which have simplified the instrument and rendered it more useful.

Figure 1 shows the machine as it stands ready for use. It is made to screw directly upon the nozzle of the carbon-dioxide tank. The valve of the latter is utilized to control the escape of the gas into the freezing stage. When the microtome is screwed directly upon the carbon-dioxide tank it is necessary that the tank should lie in a horizontal position, on a table for instance, where it may be held in place by some simple clamp. On the other hand, if it is desired to connect the microtome to a tank placed in some other than the horizontal position an L-shaped piece of tubing may be screwed on the nozzle of the tank and the microtome on the other end of the L tube. The tank may then be placed in any position desired.

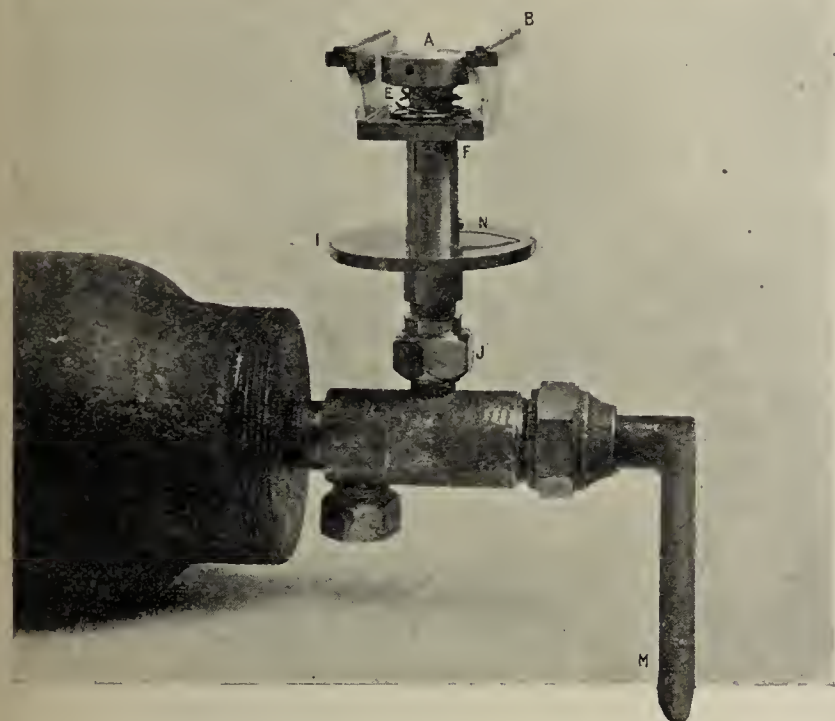


FIG. 1.

- A. Cover of freezing stage.
- B. Glass track for carrying knife.
- E. Spiral spring.
- F. Tubal base of knife-stage.
- I. Wheel.
- J. Nut for attaching axial tube to tank.
- M. Handle of tank-valve.
- N. Pointer.

The axis and main support of the machine consists of a solid tube with a narrow lumen (*K-D*, Fig. 2). This axial tube is united by a nut (*J*, Fig. 1 and Fig. 2) either to the nozzle of the tank or to the L-shaped tube mentioned above.

The machine is thus very readily attached.

On the top of the axial tube the freezing stage (*A*, Fig. 1, *A-C*, Fig. 2) is screwed. This stage piece consists of two parts, a base and a cover. The base is the part screwed into the upper end of the axial tube (*C*, Fig. 2). To this base the cover-piece is screwed (*A*, Fig. 2). Between the base of the stage and the axial tube is placed a thin brass plate

(*D*, Fig. 2) with a very narrow aperture at its centre. Through this narrow aperture the carbon-dioxide escapes into the lumen of the stage piece (*C*, Fig. 2). The difference in pressure on the two sides of the brass plate causes a very rapid expansion of gas between the cover and base of the freezing stage. The passage open for the escape of gas from the lumen of the base (*C*, Fig. 2) to the external world is in the form of a spiral passage which finally opens out through the side of the cover, as shown in (Fig. 1, *A*). Between the cover and base of the freezing stage an asbestos washer is placed. The expanding gas therefore can absorb little heat from the base of the stage. Almost all heat absorption must take place from the cover. This heat absorption is greatly facilitated by the metallic spiral which projects down from the cover so as to give rise to the spiral passage through which the gas escapes.

Through the mechanism here described far the greater part of the heat-absorbing power of the expanding gas is utilized

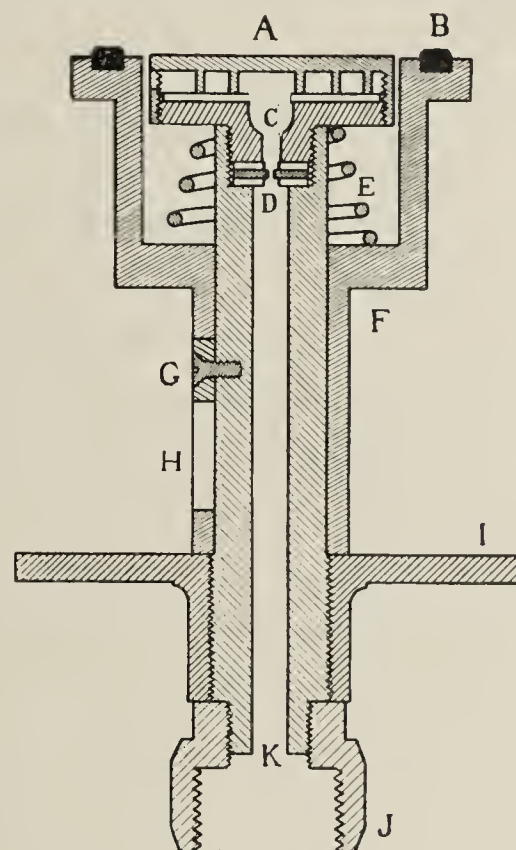


FIG. 2.

- A. Cover of freezing stage.
- B. Glass track for carrying-knife.
- C. Aperture in base of freezing stage.
- D. Aperture in thin brass plate.
- E. Spiral spring.
- F. Tubal base of knife stage.
- G. Check for limiting movements of knife-stage.
- H. Groove for G.
- I. Wheel.
- J. Nut for attaching axial tube to tank.
- K. Opening into lumen of axial tube.

to lower the temperature of the surface of the cover of the freezing stage. The temperature of the rest of the machine is but little altered. Good control of the temperature of the freezing stage can be thus maintained. This control is farther rendered possible by the valve of the tank. If this valve is turned on full the temperature of the cover of the freezing stage is quickly reduced to a very low point. Tissue placed

on it is quickly frozen. On the other hand, if the gas is not allowed to escape from the tank with full force the difference in pressure in the two sides of the brass plate is less and heat absorption from the cover is less marked. In this way tissues placed on the cover may be slowly frozen without subjecting them to severe cold. Thus, too, a constant low temperature may be maintained by opening the tank-valve to the required point.

The mechanism for controlling the thickness of the sections is equally simple. On the lower end of the axial tube a movable wheel (*I*, Fig. 1 and Fig. 2) is placed. This wheel moves up and down the axial tube on a screw thread cut twenty-five threads to the inch. A complete revolution of the wheel therefore raises or lowers it a millimeter. The margin of the wheel is divided into fifty spaces, each of which therefore represents twenty microns. A pointer (*N*, Fig. 1) serves to indicate the number of spaces passed in a partial revolution of the wheel and thus to show the thickness of the sections cut.

The knife-stage (*F-B*, Fig. 1 and Fig. 2) consists of a tubal

base (*F*), which surrounds the axial tube and rests on the movable wheel; and of two flanges (*B*) which extend above the freezing stage on each side for the support of the cutting blade. The base of the knife-stage is moved up the axial tube by screwing the wheel upwards. It is forced down the axial tube by the spring (*E*, Fig. 1 and Fig. 2) whenever the wheel is turned so as to be carried downwards. The flanges of the knife-stage support parallel glass tracks upon which the cutting blade is carried to and fro.

For cutting sections a razor or a plane or almost any good steel blade with a straight edge may be used.

The advantages of the machine are as follows:

1. But little carbon-dioxide is wasted.
2. The temperature of the freezing stage can be controlled.
3. Owing to the nature of its attachment to the tank it can be readily carried about. This should render it of especial value to surgeons.
4. Above all it is simple in design, strong, and unlikely to get out of order.

NOTES ON CERVICAL RIBS.

BY CLINTON E. BRUSH, JR.

(From the Anatomical Laboratory of the Johns Hopkins University.)

Although many cervical ribs have been described heretofore, the following description of three cases is given because of variations presented which, while most of them have already been recorded, are somewhat rare.

CASE I. Fig. 1. The dissection of this subject was nearly completed before the cervical rib was noticed, so that most of the soft parts had already been removed before it came to my hands.

There was a cervical rib on each side, the left being much better developed than the right. Each rib was made up of head, neck, tubercle and shaft. Each articulated with the seventh cervical vertebra on the body and on the transverse process. There was a simple stellate ligament at the costo-central articulation, and a capsular ligament at the articulation of the tubercle with the transverse process.

The left rib extended down to the upper border of the first thoracic rib, with which it articulated, being held in position by a capsular ligament. There was a slight articular eminence or facet on the first thoracic rib at the point of articulation, the facet apparently corresponding to the scalene tubercle of a normal first thoracic rib. The left cervical rib projected a distance of 2.3 cm. beyond the body of the seventh cervical vertebra and then curved sharply downwards. The extreme width of the rib was at this point, where it measured 1.6 cm. The shaft of the rib was triangular in cross-section and measured .4 cm. in thickness.

The seventh cervical nerve on the left side crossed the middle of the broad upper half of the rib in a well marked groove.

At a point 2.6 cm. from the distal end of the rib was the superior border of a sharply defined groove, .9 cm. in width. Across this passed the lower trunk of the brachial plexus (1), the eighth cervical and first thoracic nerves uniting before crossing the rib. As the trunk of the brachial plexus was

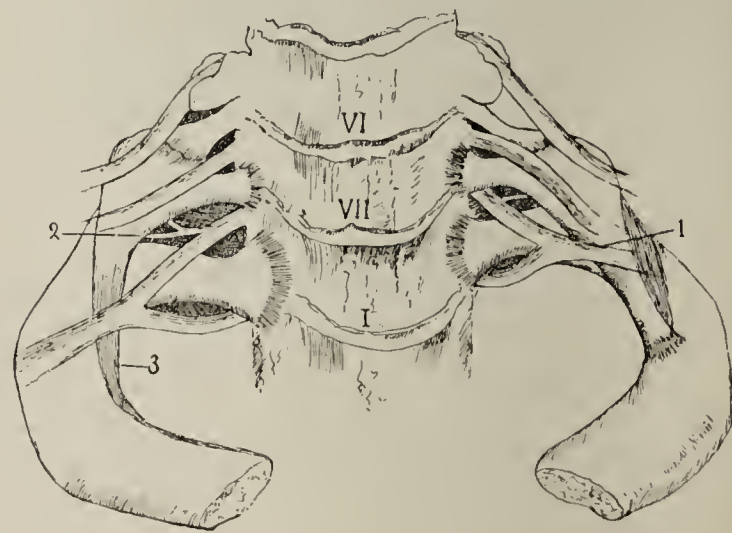


FIG. 1.

CASE I.—1. Lower cord of brachial plexus. 2. Supplementary intercostal nerve. 3. Fibrous cord.

but .4 cm. in diameter, it is probable that the subclavian artery also crossed in this groove.

In the supplementary interspace there were some well developed muscle fibres, but their condition was such that it was impossible to decide whether or not there had been both an inner and an outer set. Just before crossing the upper border of the first thoracic rib, the eighth cervical nerve

gave off a small branch (2), which divided into several smaller twigs to innervate the supplementary intercostal muscle.

The right cervical rib corresponded very closely in size and shape to the upper half of the left rib. It extended 1.7 cm. beyond the body of the seventh cervical vertebra and was 1.4 cm. wide. The upper border curved sharply downwards and met the lower border 2.6 cm. below the tubercle, so that the rib ended in a point. From this pointed end a round, fibrous cord (3) extended to the first thoracic rib, meeting it at a point corresponding to the place of articulation of the left cervical rib with the first thoracic rib on the left side. From here the fibrous cord was continued along the superior border of the first thoracic rib to the sternum.

On the right side also the supplementary interspace contained well developed muscle fibres, the nerve supply being similar to that on the left side.

The distribution of the arteries that were still on the subject was normal, except that on both sides the vertebral arteries passed up to enter the foramina of the transverse processes of the fifth cervical vertebra.

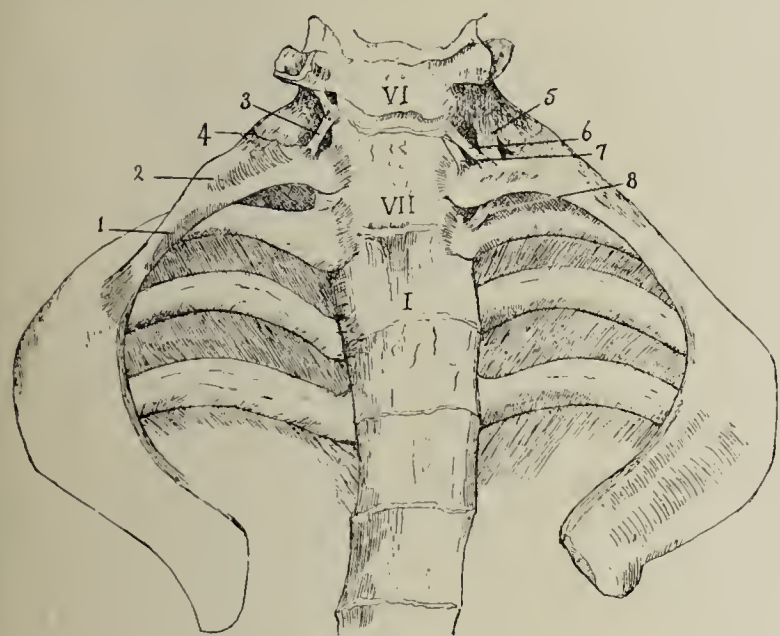


FIG. 2.

CASE II.—1. Groove for subclavian artery and lower cord of brachial plexus. 2. Groove for VII cervical nerve. 3. Ligament. 4. Capsular ligament. 5, 6, 7 and 8. Ligaments.

CASE II. Negro woman. Age, about 60 years. Fig. 2. Vertebral formula—*C*, 7; *T*, 12; *L*, 5; *S*, 5.

This subject possessed two well developed cervical ribs, that on the left side being much better developed than that on the right. Each rib consisted of head, neck, tubercle and shaft. Each articulated with the seventh cervical vertebra in two places—the body and the transverse process. The right rib articulated with the superior border of the first thoracic rib, 6.9 cm. from the head of the latter. The left rib was ankylosed with the superior border of the first thoracic rib, the central point of the ankylosis being 5.5 cm. from the head of the thoracic rib.

The general shape of the two ribs was the same, the upper part of the shaft being broad and flat and then rapidly narrowing down to a shaft which was triangular in cross-section.

Each rib presented two grooves. One (1) which was very well defined, was on the anterior surface of the narrow part of the shaft for the passage of the lower trunk of the brachial plexus and the subclavian artery. The other groove (2) was very slight and extended outward across the broad upper part of the shaft for the passage of the seventh cervical nerve.

The diameter of the first thoracic rib on the left side from its head to the ankylosis with the cervical rib, but more especially in the neck, was much less than that of the right thoracic rib in the same part. Beyond the ankylosis it was about the same width as the right rib was beyond its articulation with the cervical rib.

From the tip of the right cervical rib a round fibrous cord extended to the sternum along the superior border of the first thoracic rib, being closely adherent to the latter. A similar cord was present on the superior border of the left thoracic rib, being continued from the ankylosis.

The principal measurements of the ribs were as follows:

	Right.	Left.
Head, neck and tubercle	2.6 cm	2.8 cm.
Straight line from back of tubercle to		
end of rib	4.7 "	4.5 "
Length along concave border	5.7 "	6.6 "
Breadth of upper part of shaft	1.3 "	1.5 "
Diameter of lower part of shaft4 "	.6 "
Diameter of neck of first thoracic rib 1		
cm. from its head95 "	.55 "

On the right side, the scalenus anticus had a normal origin, but was inserted on the tip of the cervical rib and on the superior border of the first thoracic rib for 1 cm. anterior to the articulation of the two ribs. The scalenus medius was inserted along the superior border of the cervical rib from the tubercle to the upper border of the groove for the subclavian artery and lower cord of the brachial plexus, 2.3 cm. from the distal end of the rib. At the lower end of the insertion some of the fibres were prolonged downwards across the inner surface of the supplementary interspace to be inserted on the upper border of the first thoracic rib for 1.4 cm. posterior to the articulation with the cervical rib. The scalenus posticus was inserted on the outer border of the cervical rib at a point 1.6 cm. from the tubercle, in connection with the scalenus medius, and thence by a fibrous band, .3 cm. wide, backward and downward to the superior border of the first thoracic rib for a distance of .5 cm. on that rib.

The supplementary interspace on the right side was filled by two well developed intercostal muscles, an outer and an inner. The external intercostal arose from the outer inferior border of the cervical rib from the head to the extreme end of the rib. The fibres extended downward and forward to be inserted along the superior border of the first thoracic rib. The fibres arising from the end of the cervical rib spread out in a fan-shaped insertion along the anterior face of the first thoracic rib for a distance of 2.5 cm.

The internal intercostal muscle arose from the inner border of the inferior surface of the rib, the fibres running downward and backward to be inserted along the inner border of the first thoracic rib for a similar distance. This muscle was

innervated by fibres from the intercostal branch of the first thoracic nerve. This branch ran along the superior border of the second thoracic rib and sent its fibres across the first rib to the supplementary intercostal muscle.

The eighth cervical and first thoracic nerves united at the inner border of the cervical rib to form the lower trunk of the brachial plexus, which crossed the rib above the subclavian artery. Just before uniting with the eighth cervical nerve, the first thoracic gave off a slender branch which descended along the inner border of the rib, behind the subclavian artery, to the lower end of the rib, where it turned upward to gain the surface, wound around the end of the rib and was distributed to the articular ligament.

The right rib articulated freely with the seventh cervical vertebra and also with the first thoracic rib. A stellate ligament held the head of the cervical rib to the vertebra. Besides this ligament there was a superior costocentral ligament (3) passing from the superior surface of the neck of the rib mainly to the lower outer border of the body of the sixth vertebra, a small slip being continued upward and outward to the anterior inferior border of the transverse process of the same vertebra. A capsular ligament (4) held the tubercle of the rib to the transverse process of the seventh vertebra.

The disposition of the soft parts of the left side was very similar to that of the right. The scalenus anticus was inserted by a fan-shaped set of tendinous fibres to the lower half centimeter of the cervical rib, and was continued along the superior border of the first thoracic rib for 1.6 cm. anteriorly. The scalenus medius was inserted along the superior external border of the cervical rib from its head to the upper margin of the groove for the subclavian artery, 2.3 cm. from the central point of the ankylosis. The scalenus posticus was inserted on the superior border of the first rib. The iliocostalis dorsi sent a slip of insertion to the external border of the cervical rib and also one to the tubercle. On the right side the slip to the tubercle alone was present.

The external intercostal muscle in the supplementary interspace was well developed. It arose from the outer border of the inferior surface of the cervical rib from its head to the ankylosis. The fibres, running downward and forward, were inserted along the superior border and external surface of the first thoracic rib for a somewhat longer distance. The internal intercostals arose from the inner inferior border of the cervical rib, from the ankylosis to the tubercle, and extended downward and slightly backward to be inserted for a similar distance along the superior inner border of the first thoracic rib. The innervation of the supplementary intercostals was similar to that on the right side—by branches from the first intercostal nerve.

The left cervical rib articulated freely with the seventh cervical vertebra, but was firmly ankylosed with the superior border of the first thoracic rib, the ankylosis covering a distance of 2.2 cm. The tubercle articulated with the transverse process of the seventh vertebra, the joint being effected by a capsular ligament, no distinct division into smaller indi-

vidual bands being noticeable. From the neck of the rib, just within the tubercle, a fibrous band (5) .5 cm. in width extended upward, backward and slightly inward to the lower posterior border of the transverse process of the sixth vertebra, and to the anterior face of the transverse process of the seventh. A small ligament (6) connected the superior external margin of the head with the lower, outer border of the body of the sixth vertebra. Just internally to this, and arising from the middle of the superior surface of the head, a band .3 cm. wide (7) extended upward and inward to the lower outer border of the sixth vertebra, the insertion being under and inside of that of the smaller slip. Posteriorly to these, another ligament, .6 cm. wide, connected the superior posterior surface of the head with the lower border of the body of the sixth vertebra. A short, tough, fibrous cord (8) extended from the inferior surface of the head of the cervical rib to the superior surface of the head of the first thoracic rib. From the upper half of the head of the cervical rib a stellate ligament extended to the body of the seventh vertebra.

The arterial distribution on both sides was normal except for the origin of the left common carotid from the innominate artery immediately after the latter left the aorta.

There was a distinct scoliosis to the left side in the upper thoracic region.

CASE III. This was simply a cleaned specimen of a rib from the anatomical museum. Nothing was known about the subject from which it came.

The specimen was that of a left first thoracic rib, having a cervical rib ankylosed with it. The ankylosis was so complete and the free part of the cervical rib so short that it would be better to class this as a bicapital first thoracic rib. Its morphology is very similar to that of the bicapital ribs described by Turner.¹ The rib presented two heads, two necks, two tubercles; and, for a distance of 1.6 cm. beyond the tubercle of the upper division, there were two shafts. That point marked the posterior limit of the ankylosis, which extended forward a distance of 4 cm. On account of the ankylosis, the rib was very broad at this part, being 2.6 cm., while the true shaft of the first thoracic rib beyond the fusion was but 1.7 cm. The two necks were separated by a space .6 cm. wide.

The principal measurements of the rib were as follows:

From tip of head to outer border of tubercle, (upper division).	3.4 cm.
“ “ “ “ “ “ (lower division).	3.6 “
Width of neck, (upper division).....	.8 “
“ “ (lower division).....	.7 “
Straight line from head of lower division to distal end of rib.	8.5 “
Length along convex margin from head of lower division to distal end of rib	19.2 “

The upper border of the rib presented two grooves, one crossing just anterior to the central point of the ankylosis and the other .7 cm. anterior to this. In the recent state the subclavian artery and lower cord of the brachial plexus undoubtedly crossed by the former, while the latter was prob-

¹ Journ. Anat. and Physiol., 1883, vol. xvii, pt. iii.

ably for the passage of the subclavian vein. Between these two grooves there was a very prominent pointed process, projecting 1 cm. beyond the upper border of the rib. The anterior margin of its base was also the anterior limit of the ankylosis. From its general direction and from the fact that there was a visible groove along the line of ankylosis, it seems probable that this represented the tip of an originally free cervical rib. In the recent state there was probably a fibrous cord extending from the tip of the process to the sternum.

SUMMARY.

Of these three cases, the first two present some uncommon variations. In the first case the innervation of the supplementary intercostals by a direct intercostal branch from the eighth cervical nerve has been described only once.² The second case shows a peculiar insertion of the serratus posticus on the first thoracic rib. This has also been described by Gruber,² but it is not mentioned as a variation in the standard

² Mem. de l' Acad. des Sc. de St. Petersburg, 1869.

text-books, nor is it spoken of by Le Double.³ This case also presents the following variations, which, so far as I can find, have not been reported heretofore: a minute branch from the right first thoracic nerve to the articular ligament between the cervical and first thoracic ribs; a ligament connecting the head of the left cervical rib with the head of the left first thoracic rib, and a ligament from the neck of the cervical rib to the lower border of the transverse process of the sixth vertebra (Fig. 2, 5). For a full list of references to the subject of cervical ribs the recent article by Phillips⁴ may be consulted.

In conclusion I wish to express my thanks to Dr. R. G. Harrison, at whose suggestion the work was originally undertaken, for his advice and assistance in my work.

³ Traité des variations des Système musculaire de l'homme. Paris 1897. Tome I.

⁴ Journ. Anat. and Physiol., 1900, vol. xxxiv, n. s. xiv, pt. iv.

ON THE PRESERVATION OF ANATOMICAL MATERIAL IN AMERICA BY MEANS OF COLD STORAGE.

BY ABRAM T. KERR, B. S., M. D.,

Assistant Professor of Anatomy, Cornell University, Ithaca, N. Y.

The preservation of the dead body and its preparation for dissection have always been problems to the teacher of anatomy. The methods of preservation are different according to the object in view; certain methods being employed when it is only desired to keep the body for the ordinary dissection; others, when special parts, systems, or regions are to be worked out; and still different methods when it is desired to store material for months or years. One great step was made in the process of preservation of anatomical material for dissection when Frederic Ruysch, the Dutch anatomist, introduced the method of embalming by means of injection. This was further developed by William Harvey and has been brought to great perfection at the present day both by the anatomists and the professional embalmers. The various methods employed in most of the principal European schools have been carefully described by Dr. Hjalmar Grönoos in the *Anatomischer Anzeiger* for September 28, 1898; and a report upon the various methods employed in America was prepared by a committee of the Association of American Anatomists and published in *Science* January 17, 1896.

The rapid development of medical education has called for the introduction of more laboratory work in the first two years of the course, and this, together with the increased tendency to concentrate medical teaching in the larger colleges, has made it necessary to collect dissecting material during the whole year and to develop methods which shall preserve it in good condition until wanted.

The method of pickling, that is, placing the body after it

is embalmed and injected into a large vat of brine or some other fluid, is being quite generally abandoned. It is replaced in some institutions by enclosing the bodies in tightly sealed boxes, in which there is an inch or more of alcohol on the bottom and the body is surrounded by alcohol vapor. In other places the use of cold is employed to keep the bodies until they are needed.

Cold is produced according to the well known law of physics, that heat is required to change a solid into a liquid, or liquid into a gas. This heat is abstracted from surrounding substances. For the preservation of cadavers the cold was produced until the past few years by the melting of ice, either alone or combined with salt. But within recent years refrigerating machinery has been so well perfected, and the cost of these machines has been so much reduced, that to-day there are ten medical colleges in the United States which have installed refrigerating plants. The principle on which these machines work is very simple. It is well known that it requires much more heat to vaporize a liquid than to liquefy a solid; thus to liquefy 1 gram of ice it requires 80 heat units, but to vaporize 1 gram of water it takes 537 heat units. Therefore in the freezing machine a volatile liquid such as ammonia or ether is used. The machines on the market to-day are mostly ammonia machines.

The first ice machine to be used to preserve dissecting material was installed by the College of Physicians and Surgeons, Columbia University, New York, and when it had been in operation long enough to show the practicability and advan-

tages of this method plants were installed by the Johns Hopkins and by the University of Pennsylvania and later by Syracuse University, Long Island College Hospital, the University of Buffalo, Jefferson Medical College, the University and Bellevue Hospital Medical College, Cornell University Medical College, New York City, and a plant is to be built this year by the Cornell University Medical College at Ithaca, N. Y.

Last April, at the suggestion of Dr. Mall, I presented before the Association of American Anatomists at Washington a very brief account of the plant installed at the University of Buffalo. At this time I wrote to the professors of anatomy in all the institutions where I knew that they had cold storage plants and asked for certain statistics in order to compare their results with those obtained by me at the University of Buffalo. From some of these which I am permitted to use, and from the articles of Dr. Mall¹ on the cold storage plant at the Johns Hopkins, and of Dr. Holmes² on that at the University of Pennsylvania, I wish to call attention to those things which it is desirable to incorporate in a plant and those which should be avoided. I desire at this point to express my thanks to the professors in the institutions named above for furnishing me with data regarding the ice machines and vaults employed by them.

There are two systems in use at the present day. In the ammonia-absorption system a solution of ammonia in water is heated, the ammonia gas passes off into a condenser where the constant distillation raises the pressure and the heat being absorbed by a stream of cold water, the ammonia becomes liquid. The liquid ammonia is conducted to the refrigerating coils, where it again becomes a gas and by thus vaporizing produces cold. The gas then passes to another chamber, where it is absorbed by a weak solution of ammonia in water, and the strong solution resulting is returned to be heated again. This type of apparatus is said to have some advantages over the other system, as its relative cheapness and lack of complicated machinery, but it is also deficient in several respects. The Long Island College Hospital is, I believe, the only medical school which has an apparatus of this kind.

The ammonia compression machine is the one most generally used to-day. This consists essentially of three parts, as shown in the figure of the plan at the Johns Hopkins University. The evaporating coils are the pipes in which the liquid ammonia changes to a gas and absorbs heat from its surroundings. The compressor is a combined suction and compression pump which draws the ammonia vapor from the evaporating coils and forces it under pressure into the cooling coils. These are long lines of pipes immersed in running water, and under the combined action of the pressure from the pump and cold from the water the ammonia gas is here reconverted into a liquid and passes again into the evaporat-

ing coils. The flow is of course regulated by valves and pres-

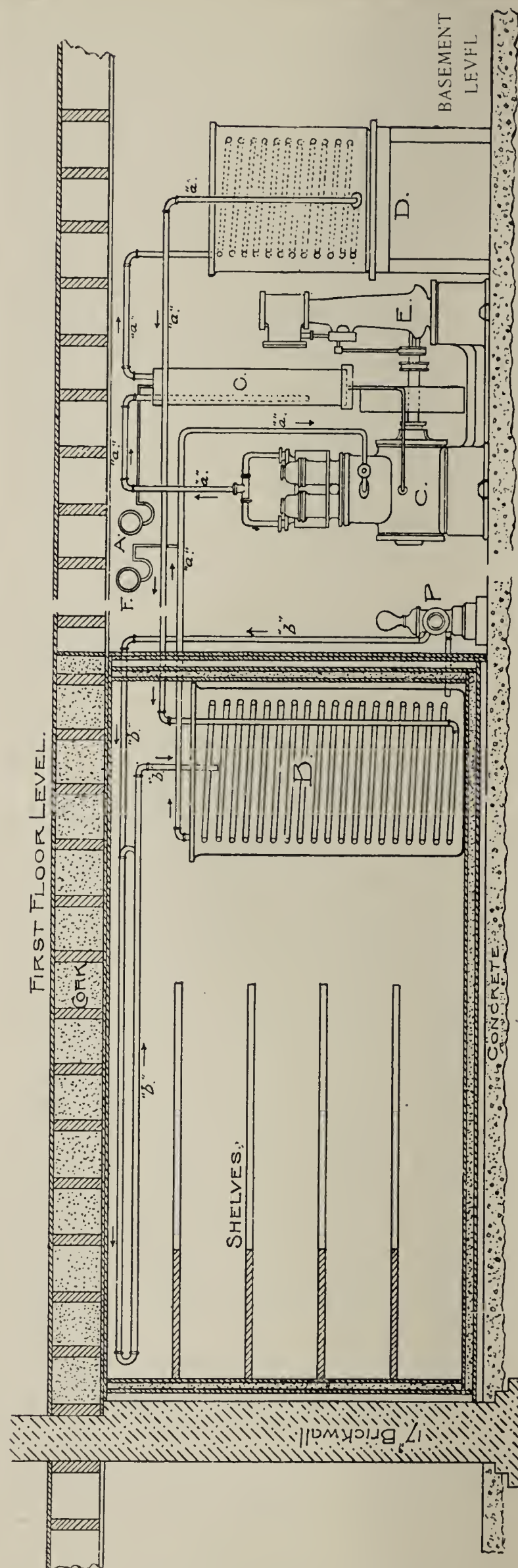


FIG. 1.—Section of the cold storage apparatus and vault at the Johns Hopkins University (after Mall). C, Compressor; D, Condenser; O, Oil Separator; E, Engine; P, Pump; B, Brine; A, Pressure Gauge; F, Back Gauge; "a," Ammonia Pipe; "b," Brine Pipe.

¹ Franklin P. Mall, The Anatomical course and Laboratory of the Johns Hopkins University, Bulletin of the Johns Hopkins Hospital, Baltimore, May and June, 1896, vol. vii, Nos. 62-63.

² E. W. Holmes, Refrigeration as a means of preservation of Bodies for use in the Dissecting room, Internat. M. Mag. Phil., 1897, vi, 747-749.

sure gauges. The compression machines are utilized in two

ways. In the one the evaporating or expansion pipes are distributed directly in the room which it is wished to cool; in the other these coils are distributed through calcium chloride brine and the cold brine is pumped through the

Machines are rated in two ways, according to their ice-making capacity, and their refrigerating capacity. The latter is usually taken as twice the former. The unit of ice-making capacity is one ton of ice at 32 degrees F. frozen from water

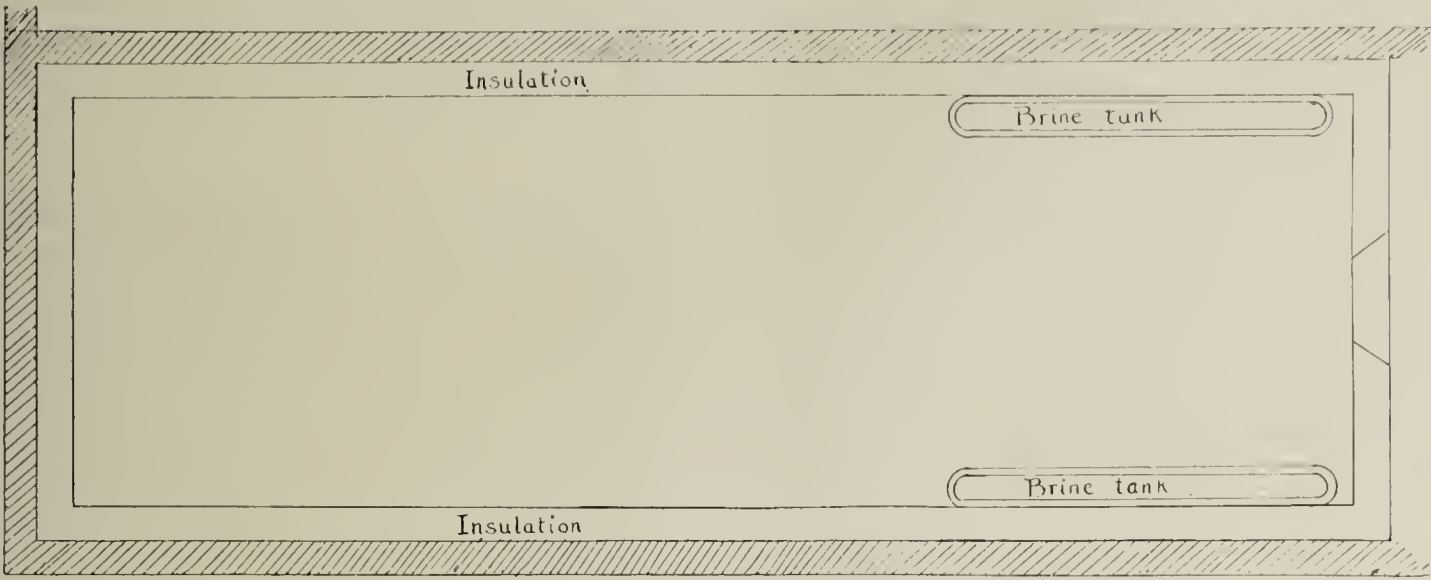


FIG. 2.—Outline of the cold storage vault at the University of Pennsylvania. The brick wall on the outside is striated.

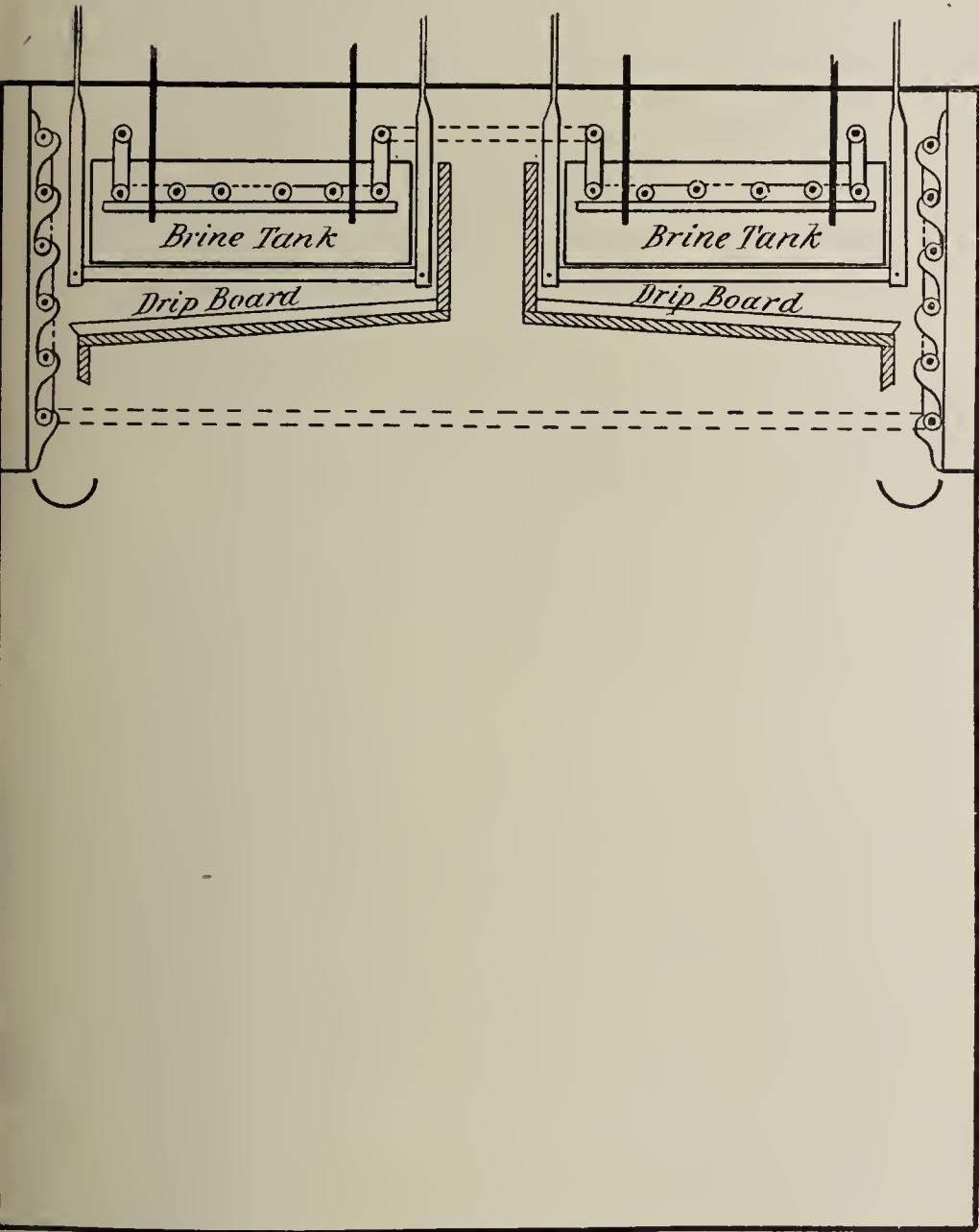


FIG. 3.—Section of the cold storage vault at the University of Buffalo.

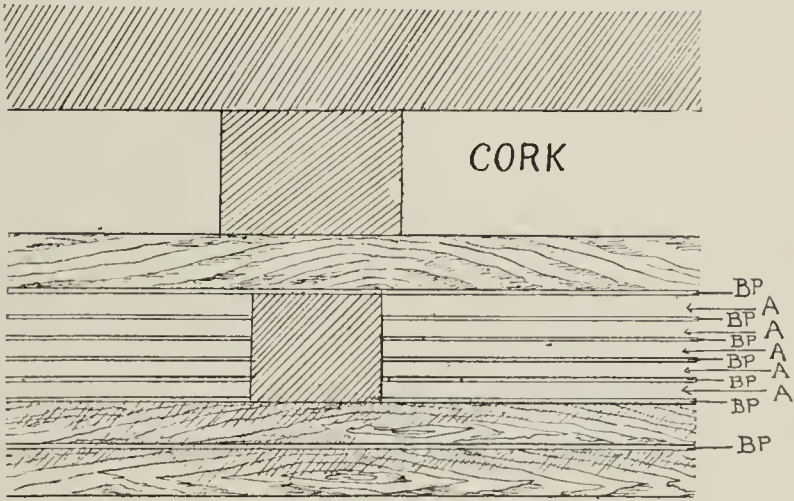


FIG. 4.—Section of the wall and insulation of the vault at the University of Pennsylvania. BP, one layer of building paper; A, half-inch air space.

rooms which it is desired to refrigerate. The first of these is known as the direct-expansion method, the other as the indirect. Johns Hopkins and Syracuse have the indirect and Pennsylvania and Buffalo the direct.

at 32 degrees F., and is equivalent to 284,000 heat units per 24 hours. It is quite important to get a machine large enough for the work required of it. The size will be influenced greatly

important that the floor should be well insulated and covered on the inside with a layer of Portland cement, asphalt or, better still, sheet zinc, which should extend up for a foot or so on the side walls of the vault. It is desirable also that the floor should slope toward the entrance, so that when the machine is shut down and the vault is being cleaned, the water will flow through the door to a drain placed in the room outside.

With a vault of a given size the capacity in bodies varies according to the method of storing them. There are three methods in general use in the different universities. The most popular is to have the vault arranged with a series of shelves. This is the method employed at the Universities of Buffalo, Pennsylvania, Syracuse and Long Island College Hospital. At the Johns Hopkins the bodies were first stored on shelves but in order to increase the capacity of the vault the shelves were removed and the bodies piled one upon an-

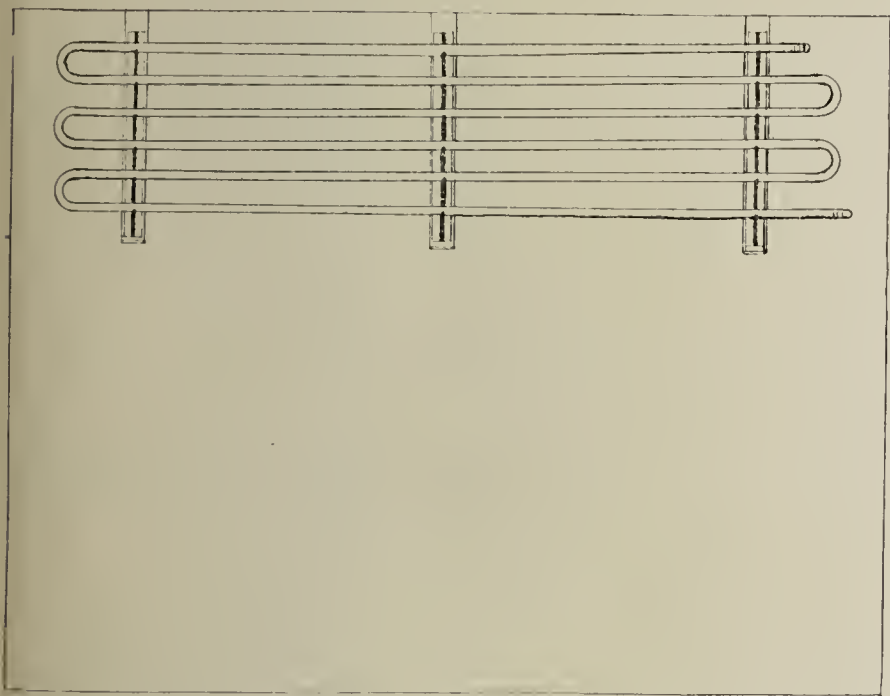


FIG. 7.—Side of vault showing the arrangement of the expansion pipes at the University of Buffalo.

other. At Columbia and Cornell, N. Y., they are suspended. There are certain advantages in each system. The method of shelving the bodies takes up the most room, but it has the advantage that each body is easily accessible. The shelves may be divided into sections and each shelf numbered, then when a body is placed in the vault the record of its position can be added to the department history and it can readily be found when desired for a particular purpose. In actual practice this works out very nicely, as employed at the University of Pennsylvania, and a body which has been stored for months and is then claimed by relatives is easily located. The shelves may be either made of slats or solid boards. The latter are used at the University of Buffalo. Where the subjects are piled one upon the other there are several advantages as well as disadvantages. First of all there is great economy of space, and the subjects being packed closely tend to prevent evaporation, but on the other hand there is a tendency for the bodies to become frozen together, causing considerable annoyance when one is to be removed. This

has been overcome by Dr. Mall by placing a layer of building lathe between the bodies after they have been vaselined and wrapped. Of course in a great pile of bodies it is very difficult to find any particular one. Bodies packed in this way tend to hold the cold for some time, so after the machine is shut down and the vault thrown open it takes several days for them to thaw out. If these bodies are piled closely around a brine tank it is still more difficult to thaw them with the additional cold from the tank, and this is a great advantage in case of a break-down.

At Columbia and at Cornell, N. Y., the bodies are suspended and run into the cold storage vault on tracks like the carcasses at a slaughter-house. I do not know the advantages and disadvantages of this method.

The temperature in the vault should not be allowed to run above freezing, as this permits thawing, and in consequence a sloppy condition of the floor. The average maximum temperature usually maintained at the University of Pennsylvania is 24 degrees and the minimum 16 degrees Fahrenheit, and at the University of Buffalo the maximum is 25 degrees and the minimum 14 degrees Fahrenheit. This is computed from the daily temperatures for June, July and August, 1899, which are given in the appended table. These temperatures are taken at the University of Buffalo by an ordinary thermometer, it being necessary to enter the vault to take the readings. At the University of Pennsylvania a self-recording thermometer takes the temperature variations.

All of the vaults are lighted by electricity, which may be turned on by a switch from the outside before entering the vault. The cost of operating a plant varies greatly, depending on the size, number of hours a day it is run, number of subjects, and also the motive power.

Steam is employed to operate the machine at the Johns Hopkins and at the Long Island College Hospital, and steam with electricity as reserve at Syracuse University. Electricity alone is used at the University of Pennsylvania, and a gas engine at the University of Buffalo. As the steam is also used for heating and the electricity for lighting it is difficult to estimate the exact amount of either used for running the machine. At the University of Buffalo and at the Johns Hopkins an estimate of the cost for one year was below \$100.

In all the cases before the body is placed in the cold room it is embalmed and the arteries filled with colored plaster, starch or at the Johns Hopkins with shellac. When wanted the body has only to be taken from the vault to the dissecting room and upon thawing it is ready for work. When a body is kept in cold storage for a time there is considerable drying of the hands and feet, face and genitals, and when kept for a long time there is a general mummification of the body. To overcome this the body is covered at the Johns Hopkins with a layer of vaseline, over which is wrapped a layer of toilet paper, and the whole is covered with cheese-cloth. The same method is employed at the University of Pennsylvania. At the University of Buffalo and at Syracuse University only the head, limbs and genitals are wrapped.

Although there are other methods of preserving the body

for dissection, it would seem that a well embalmed body properly wrapped and kept in cold storage furnishes the cleanest, best preserved and most satisfactory dissecting material. Besides being used to preserve cadavers the refrigerating plants in the different medical schools are used to keep such material from the slaughter-house as is used for dissection. Fresh organs from post mortems are also preserved in the vault until wanted, or a separate compartment, cooled by the same machine, is built to contain them.

From the study of the various cold storage apparatuses for the preservation of anatomical material it appears that the system at the Johns Hopkins is the most economical, as it does not require continuous operation of the machine. This system is further improved at the University of Pennsylvania and at the University of Buffalo for the direct system of cooling the vault at the same time the brine tank within the vault is chilled makes the pumping of brine unnecessary.

TABLES OF RESULTS OBTAINED DURING JUNE, JULY AND AUGUST, 1899 AT THE UNIVERSITY OF BUFFALO.

The machine was operated only during the day, the numbers below 12 are A. M., and those after 12 are P. M. The temperature is given in degrees Fahrenheit.

Date.	Duration of Run.	Time.	Maximum Temp.	Time.	Minimum Temp.
1899.					
June 1	4 hrs.	10	24°	1	16°
2	3	10	22	1	14
3	3¼	9	22	12	12
4	3	9	26	12	16
5	2¾	9	24	12	14
6	3	9	24	12	14
7	3	9	24	12	14
8	2¾	9.15	24	12	14
9	2¾	9.15	24	12	15
10	4	8	23	12	12
11	Sunday.				
12	3¼	8.45	28	12	17
13	2¼	8.45	26	11	12
14	3	9	26	12	16
15	3¼	8.50	26	12	16
16	3	8.45	26	12	16
17	4¼	8	24	11	13
18	Sunday.				
19	3	9	29	12	17
20	3¼	9	26	12	16
21	3¼	9	25	12	17
22	3¼	9	26	12	17
23	3¼	9	24	12	14
24	3	8	24	12	14
25	Sunday.				
26	3	9	30	12	19
27	3	8	28	12	16
28	3¾	8	26	11	15
29	4	8	26	12	15
30	Engine out of order.				
July 1	4½	8	31	12	14
2	Sunday.				
3	{ 4¼	8	31	{ 12	18
	{ 3			{ 5	13
4	Holiday.				
5	4	8	28	12	18
6	3¾	8	26	12	16
7	4½	8	26	12	16
8	4¾	8	25	12	15
9	Sunday.				
10	3	8	30	11	18
11	3¼	8	27	11	16
12	3¼	8	26	12	15
13	3½	8	27	12	15

Date.	Duration of Run.	Time.	Maximum Temp.	Time.	Minimum Temp.
1899.					
July 14	3¾ hrs.	8	24°	12	15°
15	4½	8	25	12	15
16	Sunday.				
17	3¼	8	29	12	17
18	3½	8	28	11	17
19	4¼	8	26	12	15
20	4	8	24	12	14
21	3¼	8	24	11	17
22	4	8	25	12	14
23	Sunday.				
24	4	8	29	12	18
25	3½	8	28	12	16
26	3½	8	26	12	14
27	3¾	8	26	12	16
28	3¾	8	26	12	15
29	4	8	24	12	13
30	Sunday.				
31	3¼	8	28	11	18
Aug. 1	4	8	27	12	17
2	4	8	26	12	15
3	3¼	8	24	11	14
4	4¼	8	25	12	17
5	4	8	25	12	13
6	Sunday.				
7	4	8	28	12	16
8	3¾	8	26	12	15
9	3¾	8	25	11	15
10	4	8	25	12	13
11	4½	8	24	1	12
12	4¼	8	22	12	10
13	Sunday.				
14	3¾	8	28	12	16
15	4	8	26	12	15
16	3¾	8	24	12	14
17	3½	8	24	11	13
18	4½	8	23	12	12
19	4	8	22	12	10
20	Sunday.				
21	4	8	26	12	15
22	4	8	25	12	15
23	4¼	8	23	12	12
24	3¾	8	23	12	12
25	3¾	8	22	11	12
26	3½	8	22	12	12
27	Sunday.				
28	3¾	8	27	12	17
29	4	8	25	12	16
30	4½	8	25	12	14
31	4½	8	24	12	12

TEMPERATURE RECORD ANATOMICAL VAULT MEDICAL DEPARTMENT UNIVERSITY OF PENNSYLVANIA.

The temperature is given in degrees Fahrenheit.

Date.	Duration of Run.	Maximum Temp.	Minimum Temp.
1900.			
Aug. 26	8 hrs.	5°	3°
27	12	9	4
28	10	10	3
29	10	10	5
30	9	11	5½
31	8	11	8
Sept. 1	11	12	6
2	10	14	8
3	11	11½	7
4	10	12½	6½
5	10	12½	8
6	9	13½	9
7	10	13½	8
8	9	13	9
9	8	14	8
10	7	14	11
11	10	15½	10
12	10	15½	10½
13	9	15½	9

Date.	Duration of Run.	Maximum Temp.	Minimum Temp.
1900.			
14	5 hrs.	14 1/2°	7°
15	8	13	7
16	6	14	9
17	0	15	15 1/2
18	15	16	8
19	13	11	5 1/2
20	10	9	5 1/2
21	9	13 1/2	10
22	7	16	10 1/2
23	9	16	9
24	9	15	12
25	8	16	9
26	8	15	8 1/2
27	8	14 1/2	9
28	10	14 1/2	8
29	19	13 1/2	11

The above table was compiled from five discs, loaned by Prof. Piersol, on which the temperature was recorded automatically. Each disc recorded a week's temperature. The number of hours during which the machine was in operation (by electricity) was estimated from the interval between the rise and fall of the temperature curve. There is an inconstant interval, after the machine has stopped, during which the temperature does not rise appreciably. This was estimated to be about one hour and has been deducted in making the above table.

TEMPERATURE RECORD OF THE BRINE AND VAULT AT THE ANATOMICAL LABORATORY OF THE JOHNS HOPKINS UNIVERSITY.

The machine was operated only part of the time, the object being to determine how well the insulation of the vault would hold the temperature below the freezing point.

TEMPERATURE IN DEGREES FAHRENHEIT.							
Date.	Outside.		Brine.		Vault.		
1895.	A. M.	P. M.	A. M.	P. M.	A. M.	P. M.	Duration of Run.
November 11....	59	69	29	25	8 hours
12....	59	62	29	25	2
13....	61	61	28	25	8
14....	62	73	11	0	26	21	8
15....	72	78	8	..	24	22	9
16....	71	78	6	5	24	20	4
17....	0
18....	63	69	14	5	27	23	6 1/2
19....	71	68	10	6	25	21	7
20....	70	73	10	2	26	21	8

TEMPERATURE IN DEGREES FAHRENHEIT.							
Date.	Outside.		Brine.		Vault.		
1895.	A. M.	P. M.	A. M.	P. M.	A. M.	P. M.	Duration of Run.
November 21....	26	28	0 hours
22....	60	29	..	0
23....	62	31	..	0
24....	0
25....	62	73	22	10	32	25	8
26....	72	78	13	2	28	23	8
27....	70	76	8	2	25	22	8
28....	0
29....	60	69	13	4	26	22	8
30....	70	76	9	0	24	21	6
December 1....	0
2....	64	76	12	0	26	21	7
3....	62	68	8	2	24	20	8
4....	56	57	27	26	0
5....	57	64	28	29	0
6....	56	62	29	30	0
7....	58	64	30	31	0
8....	0
9....	60	66	32	32	0
10....	58	67	25	8	32	23	8
11....	59	70	11	1	26	27	8
12....	60	64	28	29	0
13....	59	62	29	30	0
14....	58	62	30	31	0
15....	0
16....	49	48	32	32	0
17....	68	78	20	8	32	24	8
18....	70	78	8	2	29	20	8
19....	70	69	29	29	0
20....	68	68	30	31	0
21....	67	69	32	32	0
22....
23....	60	74	20	6	32	23	8
24....	72	78	11	2	27	21	10
25....
26....	76	74	8	2	27	20	10
27....	72	78	28	29	0
28....	74	78	30	31	0
29....	0
30....	68	..	18	..	32	..	8
31....	66	..	7	..	25	..	8
1896. January 1....	0
2....	68	72	28	29	0
3....	68	74	29	30	0
4....	64	68	30	31	0
5....	0
6....	58	60	32	32	0
7....	60	62	32	32	0
8....	64	67	20	8	32	25	8 1/2
9....	68	72	11	2	27	20	10
10....	66	68	28	29	0
11....	68	70	29	30	0
12....	0
13....	61	68	31	32	0
14....	68	74	18	3	32	22	10

ON THE DEVELOPMENT OF THE NUCLEI PONTIS DURING THE SECOND AND THIRD MONTHS OF EMBRYONIC LIFE.

By MARGARET LONG.

(From the Anatomical Laboratory of Johns Hopkins University.)

This work was undertaken in the fall of 1899 at the suggestion of Doctor Barker, and has been carried out with his assistance. The specimens used are human embryos and were very kindly lent by Doctor Mall from his collection.¹

¹ The numbers of the embryos correspond with their numbers in the embryological cabinet of the Anatomical Laboratory of the Johns Hopkins University.

The following embryos are described in the order of their probable age, as estimated by their length and by the development in the rhombencephalon. The arrangement of the cerebral nerves and the general appearance of the medulla oblongata agree with the His models and with the description given by His in "Die Entwicklung des menschlichen Rautenhirns"; a description of these is accordingly unneeces-

sary. Each embryo has been studied in serial sections and from these sections a few, at different stages of development, have been selected as characteristic of the structure of the pons, its nuclei and fibres. To make the work complete it will be necessary to study more embryos at intermediate stages between the five given here, and others from the third month up to the adult pons.

Embryo No. LXXV is 30 mm. long and has been cut into serial sagittal sections. The nuclei, which I have designated as "B," "C," "D," "E" and "H" in the various sections, are masses of cells distributed through the ventral part of the mantle layer (Mantelschicht of His) at or near the level of the pontal flexure. The most medial of these nuclei extend to within 0.7 mm. of the middle line. An unstained fibre bundle can be seen on the surface of the rhombencephalon ventral to the mantle layer throughout its entire length.

Section No. 73 is 2.1 mm. to the left of the middle line (Fig. 1). Near the ventral surface on the cerebral side of the nervus trigeminus is a well defined cell-mass, "B." On the ventral surface opposite the nervus acusticus is a deeply stained cell-mass, "H," which (when followed in the series) is seen to extend lateralward and spinalward to the floor of the fourth ventricle at the junction of the latter with the telachorioidea. The section of the mantle layer presents longitudinal striations which have a slight ventral convexity. A few of these strands are more deeply stained than the rest between the level of the N. trigeminus and that of the N. acusticus. The dark ependymal epithelium and the unstained ventral fibre bundle are evident.

Section No. 91 is 1.2 mm. to the left of the middle line. On the ventral surface of the pons is a delicate shell or mass of cells, "H," continuous lateralward with "H" of the previous section. Between it and the mantle layer is the ventral fibre bundle. Dorsal from "A" is a cell-mass, "C," partially subdivided by a few colorless dorsoventral stripes; ventralward and cerebralward from "C" is another mass, "D," and still more cerebralward and dorsalward are two small deeply stained cellular masses, "E." The mantle layer of the medulla oblongata is deeply stained. It contains a diamond-shaped mass, "S," spinalward from "C," the longitudinal striations mentioned in the previous section, and an unstained dorsal fibre bundle (DF).

Section No. 96 is 1.05 mm. to the left of the middle line. "H" and "C" are still present. The ventral fibre bundle passes partly along the dorsal surface of "H" and partly between "C" and "E." Just cerebralward from the pontal flexure, close to the floor of the ventricle, is "M," an oval mass of cells with a clear unstained area behind at its spinal end, and measuring 0.8 mm. in transverse diameter. The appearance of the mantle layer is the same as before. In its dorsal and cerebral part is seen an unstained dorsal fibre bundle.

Embryo No. LXXXVI is 30 mm. long and has been cut into serial coronal sections. There is ventralward a definite mass which I have designated as the nucleus pontis ventralis; it is about 1 mm. long by 3 mm. wide. The raphe enters

this nucleus in the middle line. Dorsal from its lateral part are several scattered masses which I have designated, tentatively, the nuclei pontis dorsales. The unstained ventral fibre bundle is dorsal from the nucleus pontis ventralis.

Section No. 175 is spinalward from the masses mentioned. On the ventral surface medialward from the nervus acusticus (NA) is the cell-mass "H." Followed through the series this cell-mass extends spinalward, dorsalward and lateralward to the ependymal epithelium of the fourth ventricle; cerebralward, it is medial to the nervus trigeminus and continuous with the nucleus pontis. Taken in order from the raphe lateralward in the mantle layer are the nucleus olivaris superior (S) and the superior olivary complex (S), the ascending and descending parts of the root of the nervus facialis, the nucleus nervi facialis (NNF), and the corpus restiforme (CR). On the floor of the fourth ventricle are the nucleus nervi abducentis (NNA) and the nucleus N. vestibuli (radicis descendens), (HRVD); further lateralward are the nuclei N. cochleæ, namely the nucleus N. cochleæ dorsalis (NRCD) and the nucleus N. cochleæ ventralis (NRCV). The unstained area is the ventral fibre bundle (VF).

Section No. 184 is 0.45 mm. cerebralward from the preceding section. In the mantle layer are seen in order the nucleus olivaris superior, (S), the nucleus nervi facialis (NNF), and parts of the ascending and descending limbs of the nervus facialis. "H" is on the ventral surface lateral from the nervus facialis. On the floor of the fourth ventricle is the nucleus N. vestibuli medialis et radicis descendens (NNV).

Section No. 202 is 0.9 mm. cerebralward from section 184. The nucleus pontis ventralis reaches lateralward as far as the nervus trigeminus. In the middle line the raphe extends from the nucleus pontis to the ependymal epithelium. The nuclei pontis dorsales consist of several irregular masses, "A," "B," "C," and "E," and a more ventral and lateral mass, "D." These nuclei extend through the pons for a distance of 0.5 mm. in the cerebrospinal diameter. Between these ventral and dorsal nuclei is the unstained ventral fibre bundle. Lateral from the nervus trigeminus are the nucleus nervus trigeminus ascendens and an unstained area.

Embryo No. XLV is 28 mm. long, and has been cut in serial sections, which divide the pons in an oblique direction in the following way: Instead of corresponding to the transverse diameter of the pons the left side of each section is further spinalward than the right side of the same section. The ventrodorsal plane of the section is also oblique, so that in each section the left half of the dorsal surface is the more lateral, but in the right half of the pons the dorsal surface is more medial than the ventral. In other words, the first section removes a small portion of the pons about the cerebral ventral corner on the left side, and at the dorsal-spinal angle on the right side.

The nucleus pontis, as seen in this series, is on the surface of the rhombencephalon and follows the curve of the pontal flexure so that it is crescentic in shape, with a ventral convex surface and cerebral and spinal ends or horns. Consequently,



FIG. 1.—Section through the pons of embryo LXXV, 30 mm. long, x 15 diameters.

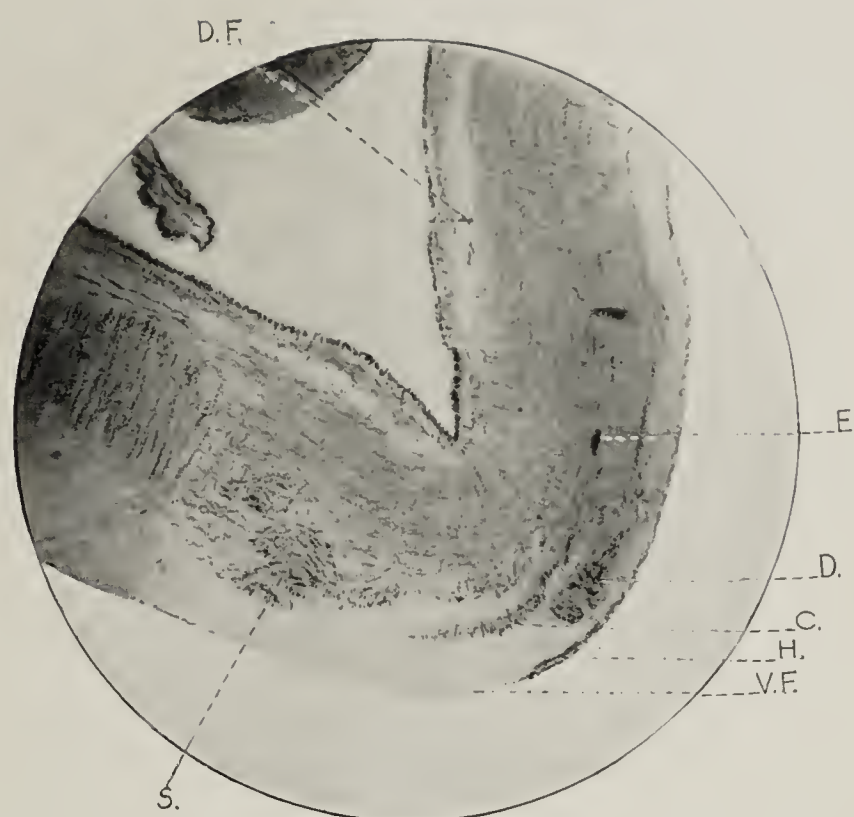


FIG. 2.—Section No. 91 of embryo LXXV, x 15 diameters.

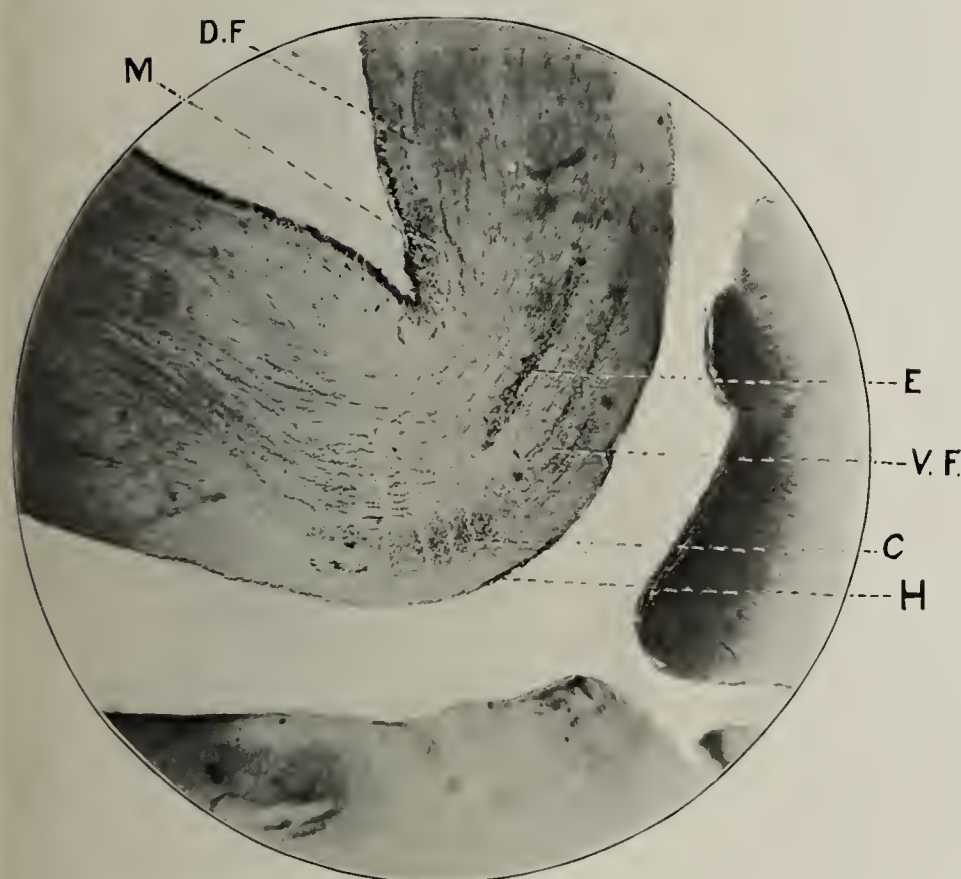


FIG. 3.—Section No. 96 of embryo LXXV.

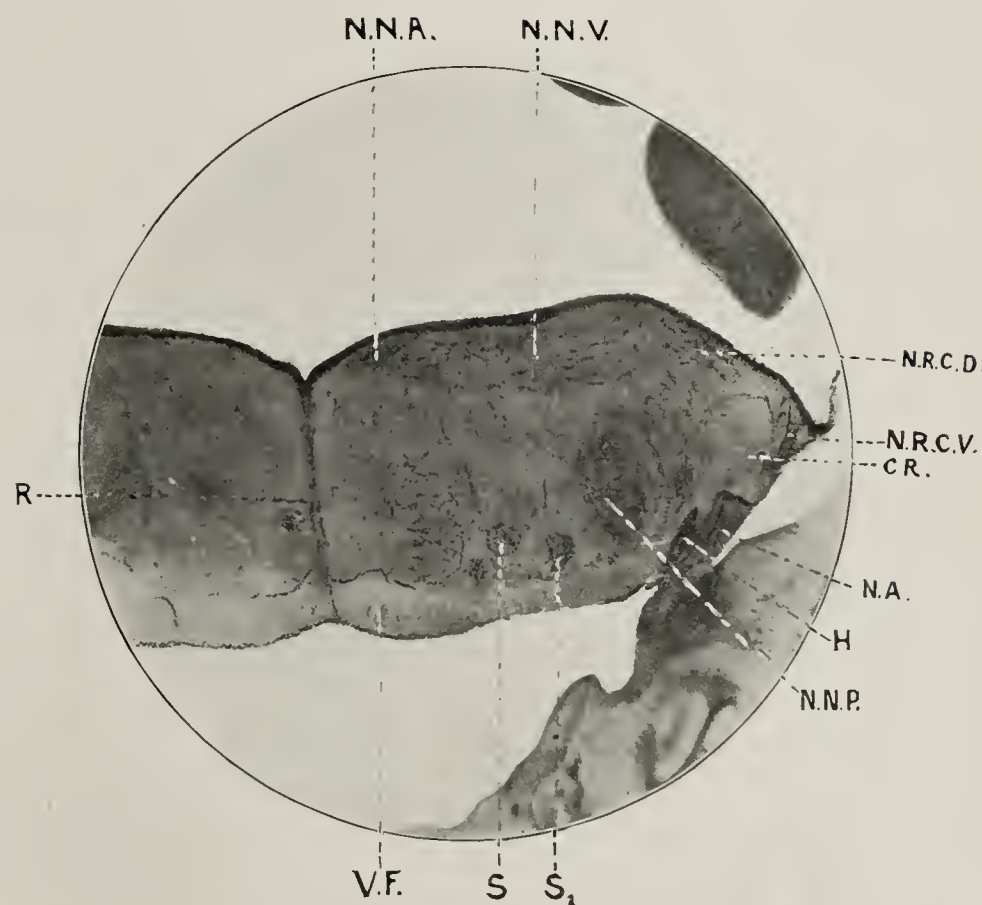


FIG. 4.—Section No. 175 through the brain of embryo LXXXVI, 30 mm. long, x 15 diameters.

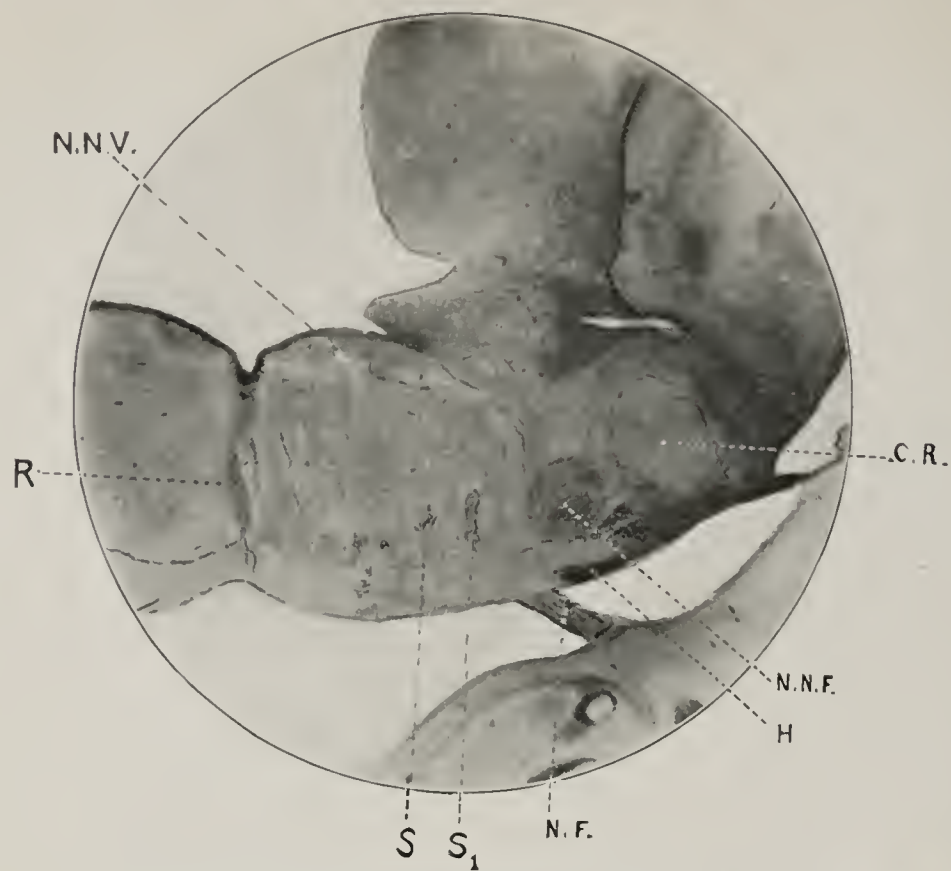


FIG. 5.—Section No. 184 through embryo LXXXVI.

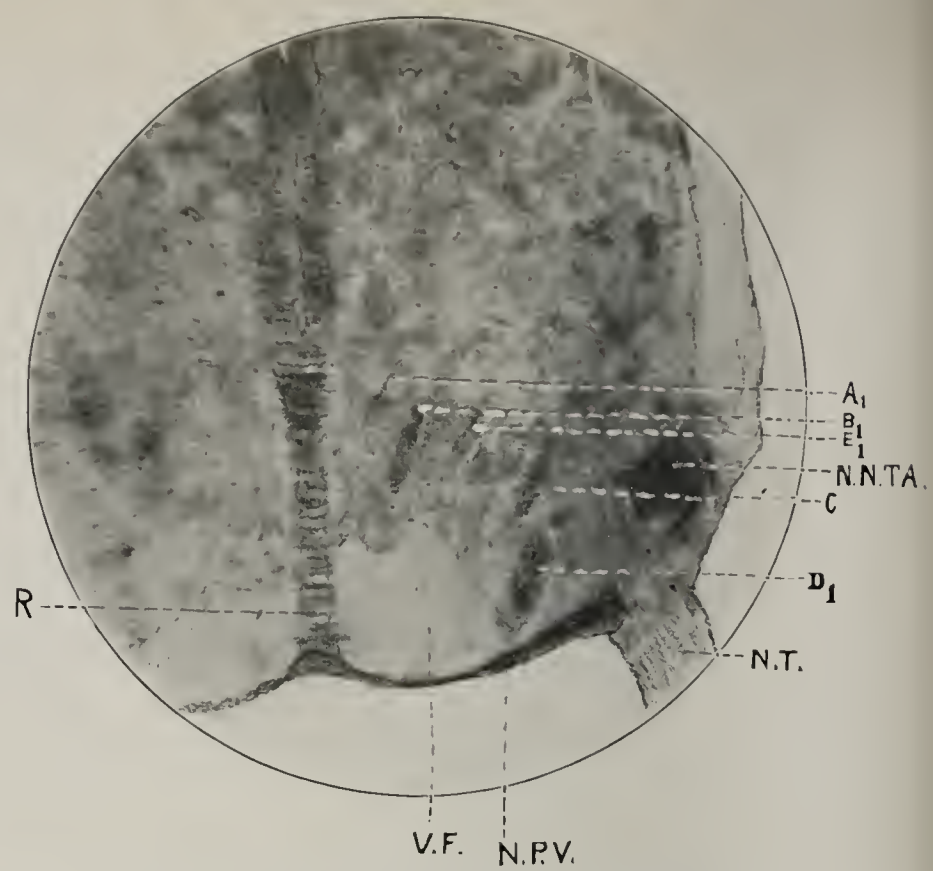


FIG. 6.—Section No. 202 through embryo LXXXVI.

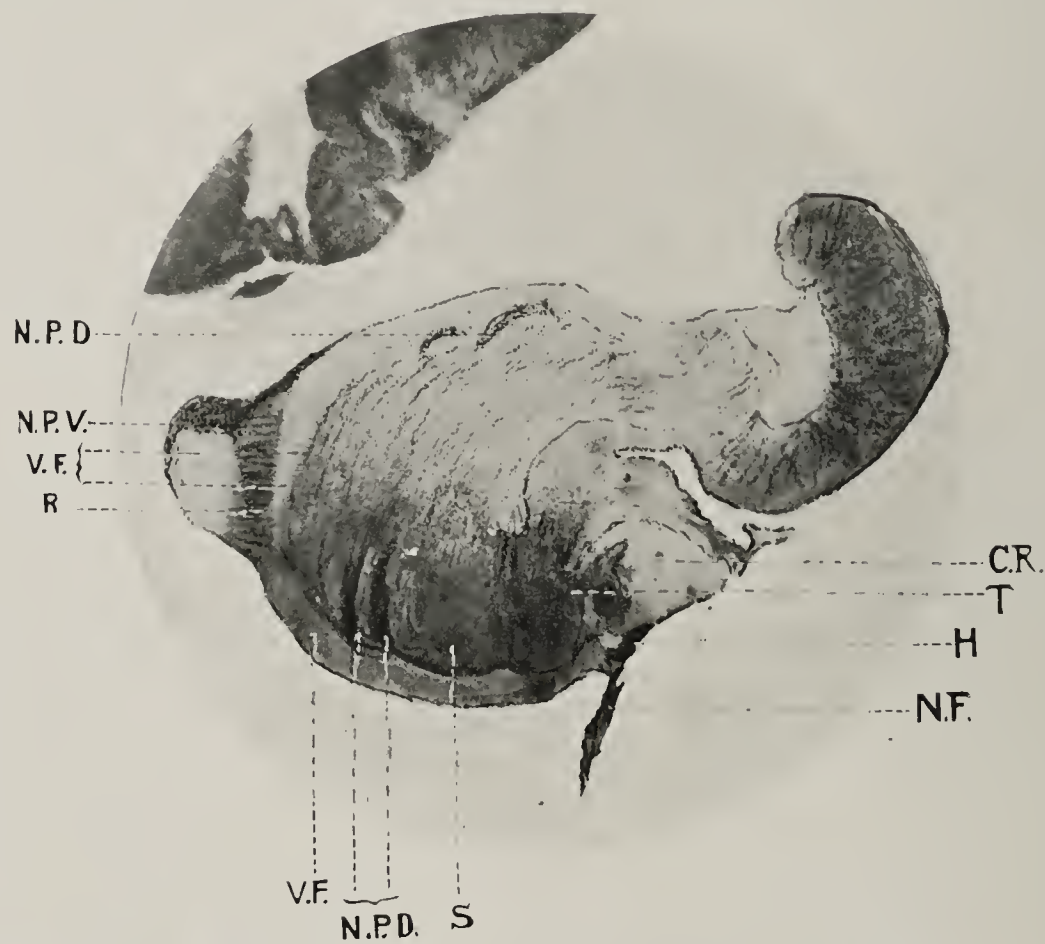


FIG. 7.—Section No. 136 through embryo XLV, $\times 15$ diameters.



FIG. 8.—Section 142 through embryo XLV.

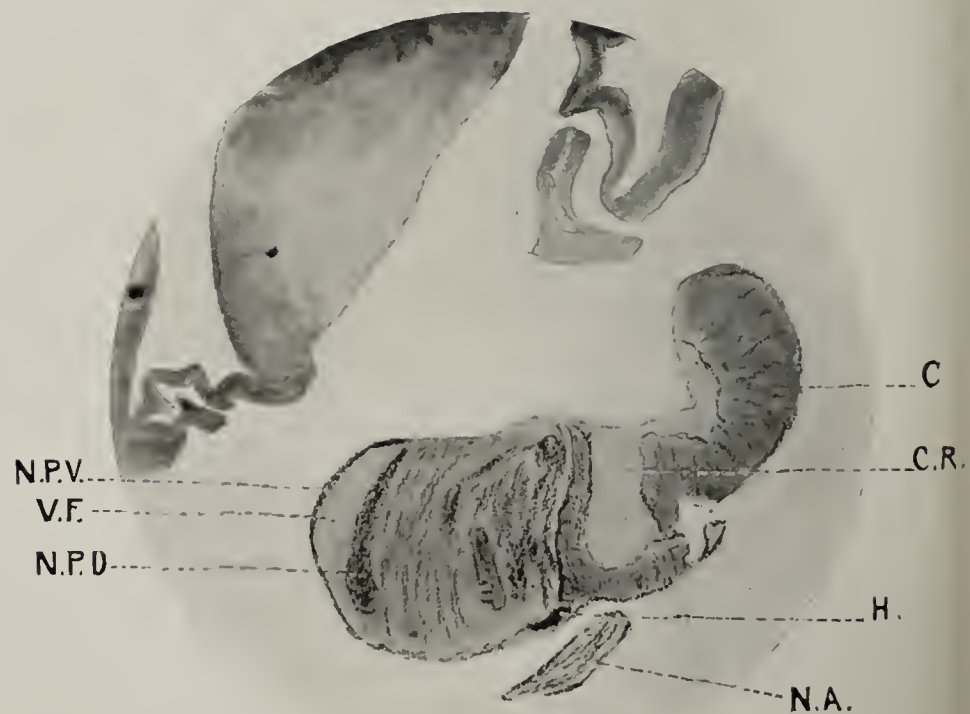


FIG. 9.—Section 145 through embryo XLV.



FIG. 10.—Section No. 92 through embryo XCV.

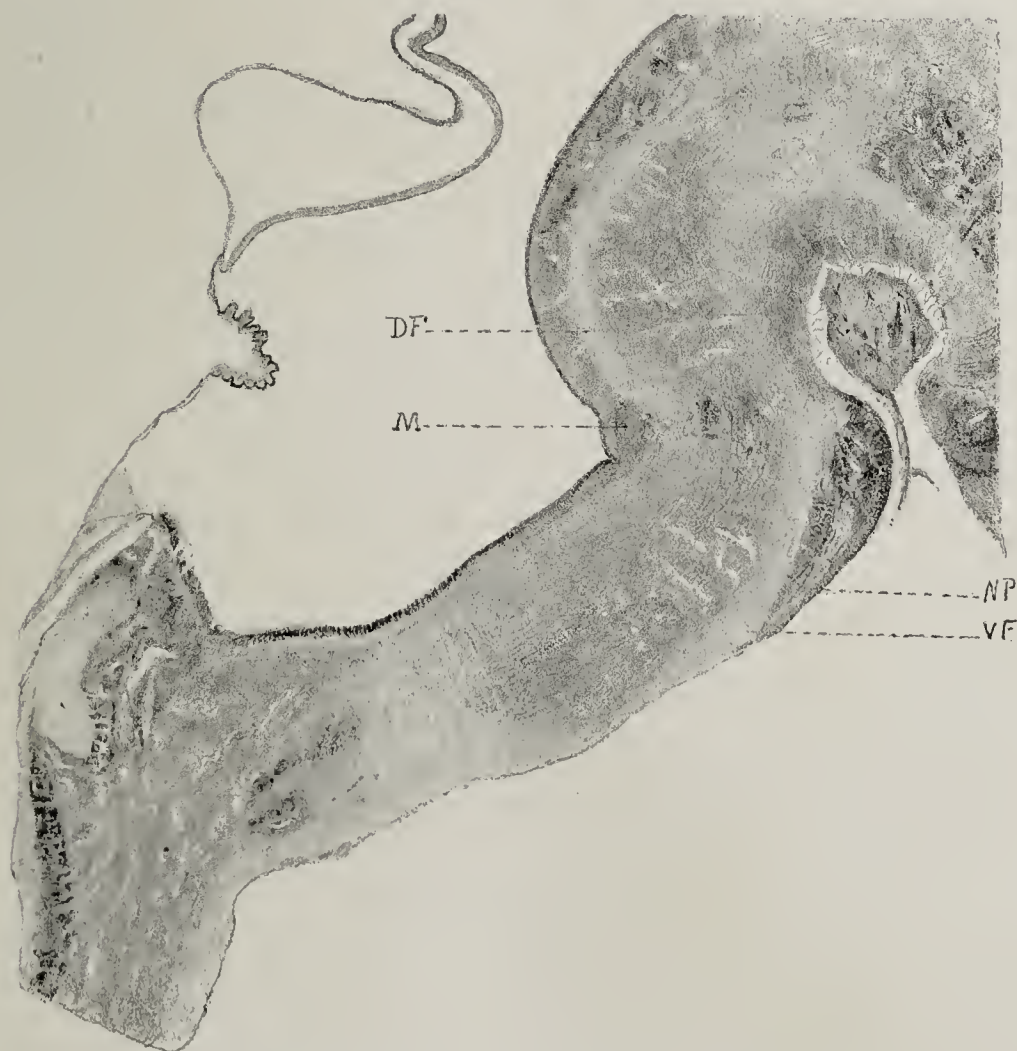


FIG. 11.—Section No. 100 through embryo XCV.

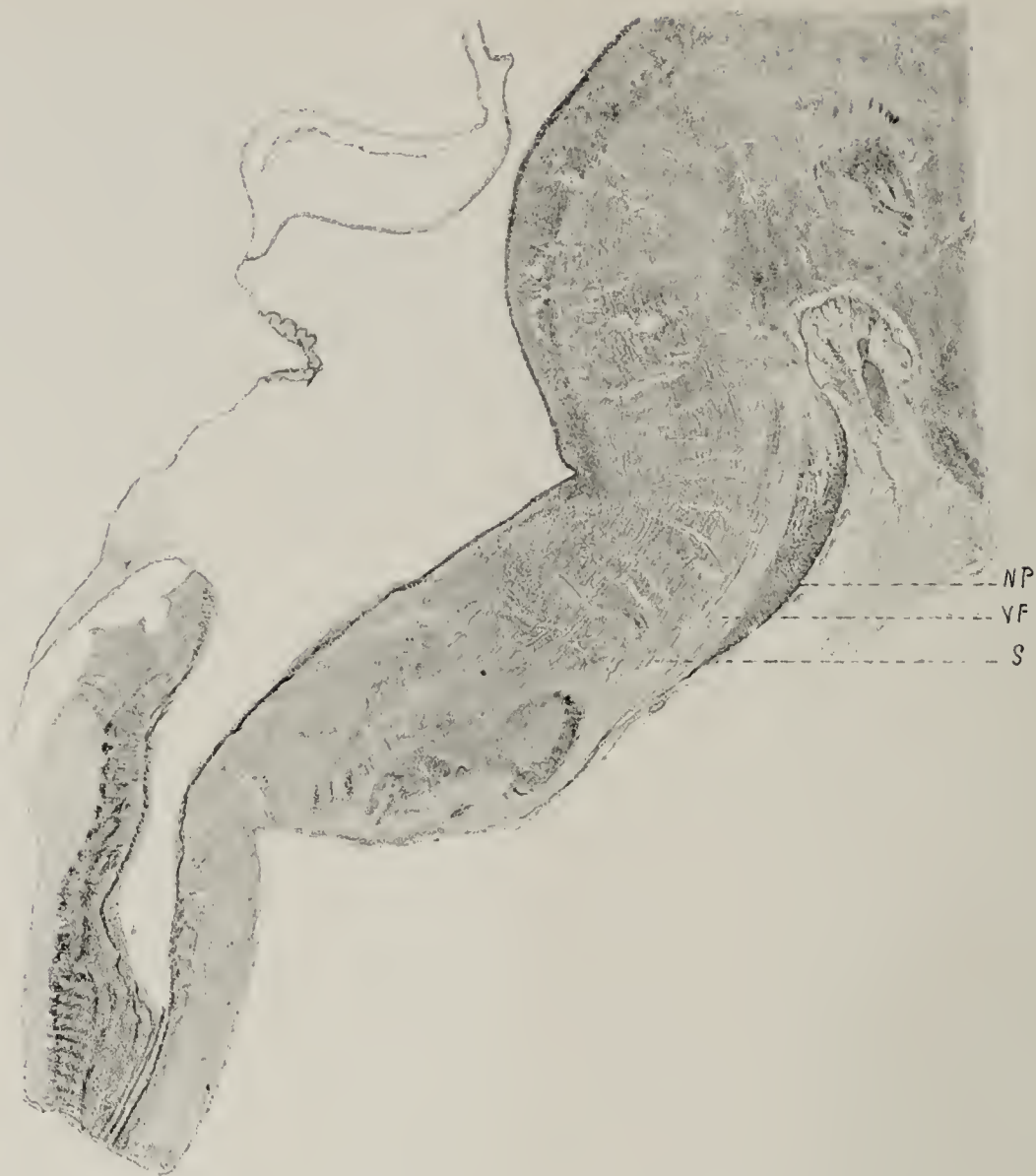


FIG. 12.—Section No. 106 through embryo XCV.



FIG. 13.—Section No. 108 through embryo XCV.

the following sections may have a ventrocerebral, a ventral, a ventrospinal and a dorsal edge.

The nucleus pontis ventralis is a solid mass of cells continuous with the raphe. The nucleus pontis dorsalis is divided into right and left halves not continuous in the middle line. The ventral fibre bundle passes between the ventral and dorsal nuclei except at their extreme lateral parts, where the cerebral ends of the two nuclei are united.

Section No. 136 is 0.05 mm. to the right of the middle line. On the right side the nucleus pontis ventralis is separated from the raphe by the ventral fibre bundle and nucleus extends across the middle line. On the left side the two ends of the nucleus pontis dorsalis are separated from the raphe by the ventral fibre bundle and mantle layer. On the ventrospinal surface at the level of the nervus facialis is a deeply stained mass of cells, "H." This mass is continuous opposite the nervus trigeminus with the nucleus pontis; spinalward, dorsalward and lateralward it extends to the ventricular epithelium of the medulla oblongata. In the medulla is a cell-mass, "T," on the medial side of the corpus restiforme, and reaching from the fourth ventricle to the ventrospinal surface. Between "T" and the nucleus pontis dorsalis is a small round mass, "S," a little more deeply stained than the rest of the mantle layer.

Section No. 142 is 2.5 mm. to the left of the middle line and shows only the left side of the pons. Between the nuclei pontis is the ventral fibre bundle. The nucleus pontis dorsalis is in the mantle layer; in its spinal end is a small unstained space. On the ventrospinal surface is the mass "H." Medial from the corpus restiforme is a round, deeply stained area "S." Near the fourth ventricle are several dark masses just like those in section 136.

Section No. 145 is 0.4 mm. to the left of the middle line. The nuclei pontis ventralis and dorsalis are continuous at their cerebral ends. Between them is the ventral fibre bundle. Opposite the radix N. cochleæ is "H," and median from it a cylindrical-shaped area. Between the cerebellum and the pons is an unstained area, the corpus restiforme.

Embryo No. XCV is 46 mm. long and cut into serial sagittal sections. The nucleus pontis is a solid mass of cells on the ventral surface of the pons, which has increased in size and measures 3 mm. in cerebrospinal, 4.6 mm. in transverse, and 0.5 mm. in ventrodorsal diameter. The ventral fibre bundle divides into two masses, the larger passes dorsal to the nucleus, the smaller through it.

Section No. 92 is 0.2 mm. to the left of the middle line. The nucleus pontis is a solid mass of cells. Dorsal from it is a dark wedge-shaped area; its ventral surface reaches as far as the nucleus pontis and extends 0.4 mm. beyond the middle line on each side, the dorsal surface is continuous with the ependymal epithelium in the middle line and for a distance of 0.3 mm. to the right. This area contains ventrodorsal markings, and small masses of cells staining more deeply than the rest of the tissue of the wedge between them. On the floor of the fourth ventricle just cerebral from the pontal flexure are two dark round cell-masses, "M," which extend through

a few sections on either side of the middle line, but in the middle line are overlapped by the greatly thickened ependymal epithelium. On the ventral surface of the medulla oblongata is the ventral fibre bundle. Near the dorsal surface cerebral from the pontal flexure is the dorsal fibre bundle. The mantle layer contains the curved longitudinal striation, and in the isthmus is more deeply stained than in the medulla, and also contains blood-spaces. Next the ependymal epithelium the mantle layer of the medulla presents a uniform appearance, and in the isthmus it contains several darker masses of cells.

Section No. 100 is 0.6 mm. to the right of the middle line. The spinal portion of the nucleus pontis is divided into ventral and dorsal parts by a clear area, containing a few dark strands composed of cells. "M" is still present; between it and the nucleus pontis are several small cell-masses. The ventral fibre bundle is on the surface of the medulla and next the dorsal side of the nucleus pontis. The mantle layer contains the curved longitudinal striation and blood-spaces. Between the dorsal fibre bundle and the ependymal epithelium are numerous dark cell-masses.

Section No. 106 is 1 mm. right of the middle line. The nucleus pontis is more unevenly stained. Its cerebral end is divided into ventral and dorsal parts by an unstained area, which is continuous with the ventral fibre bundle. The fibre bundle extends the entire length of this section. It is now seen that this fibre bundle has an oblique direction through the cerebrolateral and spinomedial portion of the rhombencephalon. The appearance of the mantle layer is the same as in the preceding section; between the nucleus pontis and the nucleus olivaris a few of the curved striations are more deeply stained than the rest, "S."

Section No. 108 is 1.4 mm. to the left of the middle line. The nucleus pontis is a smaller mass, unevenly stained owing to the presence of large numbers of white spots (nerve-fibres). Dorsal from it is the ventral fibre bundle. The mantle layer appears as before but the mass "M" is not present. Between the nucleus pontis and the nucleus olivaris are a few small cell-masses, and several more are scattered throughout the mantle layer of the isthmus.

Embryo No. XCVI is 48 mm. long and cut into serial sagittal sections. The nucleus pontis has increased in the ventrodorsal diameter. The appearance of this specimen is almost identical with that of No. XCV, and is only of interest because it corroborates what was found there. So I have not thought it necessary to add illustrations. Just spinal from the nervus trigeminus the nucleus pontis is continuous with a mass of cells which reaches to the ependymal epithelium of the fourth ventricle. The ventral fibre bundle passes partly along the dorsal surface of the nucleus pontis, and partly through it. Among the latter fibres are a few scattered strands of cells resembling more the appearance of the pons at later stage. The wedged-shaped area and the cell-mass appear as before.

The histological structure of these specimens is as follows: The ependymal epithelium contains large, dark, densely

packed, round and oval cells. The mantle layer in the earlier stages consists of round cells and a few oval cells. In embryo No. LXXV an unstained fibrous network is seen and the round cells are scattered through it, which in No. LXXXVI and No. XLV are more closely packed together. In the older specimens neuroblasts of the mantle layer point in various directions, a good many of them direct their axones ventralward, and many round cells are still seen. Most of the neuroblasts are now arranged in definite groups; between them is an unstained fibrous network which contains spongioblasts. Both the nucleus pontis and the mass "M" are composed of round cells in all the sections. The mass "H" consists of round cells, resembling in size and staining reaction those of the ependymal epithelium. The raphe appears in two specimens; it consists of fibres which interlace across the middle line, round cells, and in the frontal sections a few oval cells with their long axis transversely directed. In sagittal sections the raphe is not seen; its fibres, if present, would be cut in cross-sections.

SUMMARY.

The main nucleus pontis is situated on the ventral surface of the rhombencephalon at the level of the pontal flexure. In the specimens the nuclei pontis are first seen on the surface

and in the ventral part of the mantle layer of the lateral part of the pons Varolii. Ventral to all, in this early stage, except the mass of cells "H," is the ventral fibre bundle. In the second embryo the nucleus pontis ventralis extends across the middle line of the rhombencephalon and the nuclei pontis dorsales are separated from its lateral part by the ventral fibre bundle. The nuclei pontis dorsales next form two solid masses, reaching almost to the middle line. They are still separated by the ventral fibre bundle from the nucleus pontis ventralis, except at the extreme lateral ends, where they are continuous with each other. Next the nucleus pontis becomes a solid shell on the ventral surface cut by a small branch from the ventral fibre bundle. After the sixth month the pons consists mainly of fibres and scattered groups of cells which increase at the expense of the dorsal part of the nucleus, while a narrow ventral nucleus or cell-mass is left on the surface.

The neuroblasts of the pons are continuous with the epithelium of the floor of the fourth ventricle:

(1) By the cell-mass "H" at the lateral end of the nucleus pontis.

(2) By the round cells in the raphe.

(3) In the middle line by the neuroblast in the wedge which connects both the ependymal epithelium and the cell-mass "M" with the nucleus pontis.

THE ARCHITECTURE OF THE GALL-BLADDER.

BY MERVIN T. SUDLER, PH. D., M. D.,

Instructor in Anatomy, Johns Hopkins University.

During the past few years the development of the surgery of the gall-bladder and ducts has increased the interest in their finer anatomy, and various investigations have been undertaken in order to add to our knowledge in regard to their structure. The lymphatics and finer blood-supply, however, do not seem to have had the same attention as the musculature and nerve supply; and so this paper deals more with this part of its structure and its histology than those which have been carefully considered in other papers.

The results mentioned here were obtained for the most part by the use of the gall-bladders of dogs and pigs. They were used because of their suitability and the ease with which they could be obtained. A limited number from cats and beeves were used also. The results thus obtained from fresh material were verified or refuted upon human gall-bladders as far as the limited supply and general bad condition of them allowed. Within a few hours after death the bile stains and macerates the tissues so that they are quite changed. The mucous membrane disappears entirely in from five to six hours after death; the nuclei and tissues under it refuse to stain, and it is impossible to obtain satisfactory results from any but the freshest material. For the histology small pieces hardened, distended and contracted in saturated

corrosive sublimate solution yielded material that stained well and gave good pictures. For the connective-tissue elements the most striking picture was obtained by the use of Van Gieson's acid fuchsin and picric acid, but Weigert's elastic fibre stain furnished the most accurate and delicate picture. For the blood-vessels ordinary carmine gelatin mass and lamp-black or cinnabar gelatin mass were all that were necessary. For the lymphatics a saturated aqueous solution of Prussian-blue proved to be the best, notwithstanding a careful trial of a number of more complicated and presumably better masses.

The thickness of the wall of the gall-bladder varies according to its state of distention. In an adult human subject it is from $\frac{3}{4}$ mm. thick in a state of distention to 2 mm. in a state of contraction. The distended gall-bladder of a newborn infant is nearly $\frac{3}{4}$ mm. thick. In the pig it may be from $\frac{3}{4}$ to 3 mm. thick, and in a dog of medium size from $\frac{1}{2}$ mm. to $1\frac{1}{2}$ mm. thick. The wall of the gall-bladder is made up of the following coats: 1. mucous; 2. fibro-muscular; 3. subserous and on the free part covered by peritoneum; 4. serous. The relative thickness of these coats can be seen in Fig. 6, which shows the gall-bladder of the dog contracted. The relations are essentially the same in man as in the dog.

The mucous layer is thrown into a series of folds from $\frac{1}{4}$ to $\frac{1}{2}$ mm. high in man. These folds of mucous membrane cover corresponding ridges of connective tissue of the fibro-muscular layer and contain an exceptionally rich capillary network. The irregular spaces surrounded by these folds are much larger at the fundus than at the duodenal end of the gall-bladder. In man the measurements in the distended gall-bladder are 3 mm. \times 5 mm. in the fundus and 1 mm. \times $\frac{1}{2}$ mm. or smaller near the beginning of the cystic duct. In the crypts formed by the folds solitary lymph follicles are found. These are more numerous in the dog than in the pig, and in this regard there seems to be a great deal of individual variation. The mucous layer is composed of simple columnar epithelium, which rests upon an incomplete muscularis mucosa. In the dog these cells are from 25-42 μ thick. These cells seem to secrete a thick mucous material but no goblet cells are present. R. Virchow (1), in an article published in 1857, finds fine fat-drops in the ends of these cells of the gall-bladder and ducts during or just after the absorption of chyle. These droplets gradually became larger and worked toward the base of the cell. He thought this fat had been lost from the liver in the secretion of the bile and was again picked up by these cells. Nothing was seen in my preparations to suggest this. Granules were often seen in the outer end or near the base of the cells, but these gave no reactions for fat. Belonging also to the mucous layer were the tubular glands. These were beautifully shown in specimens stained in gold chloride. There are few of them in the dog, but in the pig, and especially in the ox, they are quite numerous.

The fibro-muscular coat is composed of smooth muscle fibres and interlacing bands of connective tissue. The direction and arrangement of these fibres has been very carefully studied by Hendrickson (2). He concluded that in the gall-bladder there are no definite layers and that the bundles of fibres interlace in all directions with the greatest number tending toward a transverse direction. According to Doyon (3), the muscle fibres arrange themselves in two methods in different animals: 1. A network with rather rounded meshes. This arrangement is found in the guinea-pig. This fact has been corroborated by Ranvier. 2. The muscle fibres are arranged into bundles which form a number of principal directions more or less plainly marked out. This is found in the dog and cat, and means about the same as the description of Hendrickson. My preparations and sections lead me to agree with Hendrickson, with the possible exception that near the fundus in the dog there is an outer and rather definite longitudinal layer. See Fig. 6. The part of this layer near the mucous membrane is composed almost entirely of connective tissue with only a few muscle fibres scattered through it, the part directly under the epithelium forming a mucosa which, however, shades off gradually and is not sharply separated from the underlying tissue. It is in this region that the thickest plexus of capillaries and intrinsic lymph channels exists. The solitary lymph follicles, to which reference has already been made, are found also here just

under the mucous membrane. Toward the subserous layer, on the contrary, the muscle fibres are collected into well developed bundles (especially so in the pig and ox) and the connective tissue is correspondingly less. Elastic tissue occurs even here, however, varying in form from fine threads to coarse bands. It is especially abundant in the neighborhood of the blood-vessels. See Fig. 6. Unstriated muscle also exists in the larger gall-ducts, and at the point where the ductus communis joins the ductus pancreaticus it becomes modified into a sphincter. This has been found by Hendrickson in man, the dog and the rabbit, and also by Helly (4) in man, and Oddi (5) in man. The fibro-muscular layer contains the larger blood-vessels, which divide into branches and thus supply the other layers. See Figs. 2 and 6.

The subserous layer is composed of dense interwoven elastic tissue bands which contain comparatively few nuclei, and therefore few connective-tissue elements. These bands form an irregular mesh-work which is denser on the side toward the serous layer. This layer is poorly supplied with blood-vessels, although there is a well developed set of lymph channels which communicate with the large superficial vessels coming from the liver. By pulling the gall-bladder apart it is possible to divide it into two layers; the separation occurring at the junction of the subserous and fibro-muscular layers. By separating injected tissues in this manner a very pretty picture of the circulation in each part can be obtained distinct from the other.

The serous layer is present only on the part covered by peritoneum, *i. e.* the fundus, the inferior surface of the gall-bladder and the outer surface of the gall-ducts. It is composed of simple flat endothelial cells from 4-6 μ thick and adds but little strength to the organ. The larger lymphatic vessels from the liver and deeper layers of the gall-bladder run between it and the subserous layer.

Brewer (6) has described in a very careful manner the way the cystic artery reaches the gall-bladder in man and the variations one would find ordinarily. He found that in 50 subjects only 3 corresponded to the type described in textbooks of anatomy. It is possible to judge from this of the great amount of variation existing in its blood-supply. The largest artery after it has reached the gall-bladder is usually found, however, on its inferior surface and on the side toward the middle line of the body. There also may be a smaller branch on the side away from the middle line. This is covered at first by peritoneum and then penetrates the outer part of the fibro-muscular layer and gives off the branches which supply the viscus. Most of the larger vessels are in the fibro-muscular layer near the dividing line between it and the subserous layer. See Fig. 6. If the needle of a hypodermic syringe be introduced into one of the smaller arteries and the mucous surface be watched while the fluid is slowly injected the arterioles and capillaries can be seen to be filled in areas about $2\frac{1}{2}$ mm. in diameter at a time from a single centrally placed artery. The capillaries under the mucous membrane are very numerous and in the folds the capillary network is especially thick. See Fig. 2. The blood from

these is collected into the veins and returned to the larger and deeper lying ones accompanying the arteries.

The subserous layer has a comparatively poor blood-supply. The arteries are small and the capillaries widely separated. Some of the capillaries run out between this layer and the serous layer, and thus provide for the nourishment of the peritoneal covering. Some veins of considerable size are also found in this layer. On the surface of the gall-bladder in contact with the liver the veins communicate with the branches of the portal vein and the arteries in part come from the hepatic artery.

The large lymphatic vessels running over the gall-bladder bring lymph from the liver and the coats of the gall-bladder. They follow the inner side of the cystic duct and end in mesenteric lymph glands in the dog. In the pig and in man we have either one or two systems of the large lymph vessels. In almost all cases both are represented but the territory may not be equally large and there is wide variation in their method of distribution. In cross-section these vessels are always flattened although the degree of flattening varies with the completeness of the injection. Sappey (7) figures a mass of them running over the gall-bladder in a manner somewhat resembling Fig. 4, but he only mentions the fact that they bring in the lymph from the liver and deeper layers of the gall-bladder. In my preparations they run down eventually on the inner side of the gall-bladder but there is usually a large vessel coming from the same side, but with the exception of one specimen figured in Plate 2, Fig. 4, which was believed to be pathological, are not as numerous as shown by Sappey.

In the subserous layer there is a network of lymph channels which empty into these larger vessels. See Fig. 7. This network is very irregular and the lymph channels vary markedly in size and shape. The picture of these lymphatics which seemed most normal was obtained by injecting carmine gelatin into the portal vein at a pressure of 80 mm. of mercury for fifteen minutes. This injects the lymphatics of the liver and in turn the larger ones over the gall-bladder, and finally these in the subserous coat in a more or less complete manner, but without any tearing or stretching of the vessels. In Fig. 2 they are represented as though the greater part lie simply on top of the subserous layer, while, as a matter of fact, they are scattered through it rather evenly.

The submucous sets of lymphatics are in the connective tissue just under the mucous membrane. However, they rarely run up into the connective-tissue folds but are at their lowest part or more frequently just at their base. The network is almost entirely absent in the denser muscular part. These were best seen by injecting aqueous Prussian-blue slowly under the mucous membrane and the injected portion was afterwards fixed and studied. In some cleared specimens the lymphatic vessels could be seen running up and joining the more superficial lymphatics of the subserous layer or directly one of the large superficial vessels as shown in Fig. 1. The lymphatic tissue belonging to this layer has already been described.

The nerve supply of the gall-bladder has been studied by Dogiel (8) and Huber (9) within recent years. The nerve supply is derived from two sources, viz., 1. the sympathetic system of ganglia and fibres connecting them, and 2. medullated fibres accompanying the large arteries. In regard to the distribution of the sympathetic fibres Huber suggests from the condition prevailing in other viscera that they supply the blood-vessels and smooth muscle of the coat. Doyon thinks these are unable to act without receiving stimuli indirectly from the great splanchnic nerve. Dogiel has figured in a beautiful manner the kinds of cells found in the sympathetic ganglia and concludes that all the varieties found in the walls of the intestines occur here also. Quite a number of medullated fibres are also found near the large arteries. Both Huber and Dogiel have noted them. The former suggests that they are sensory fibres and are distributed to the mucous membrane. Their termination, however, has not yet been settled by direct observation.

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DESCRIPTION OF PLATES XXV-XXVI.

FIG. 1.—The gall-bladder of a pig; natural size. The lymphatics were injected by placing the needle just under the peritoneal covering of the liver near the edge of the gall-bladder at (N). The blurred mass in the centre represents the injection mass showing through and the

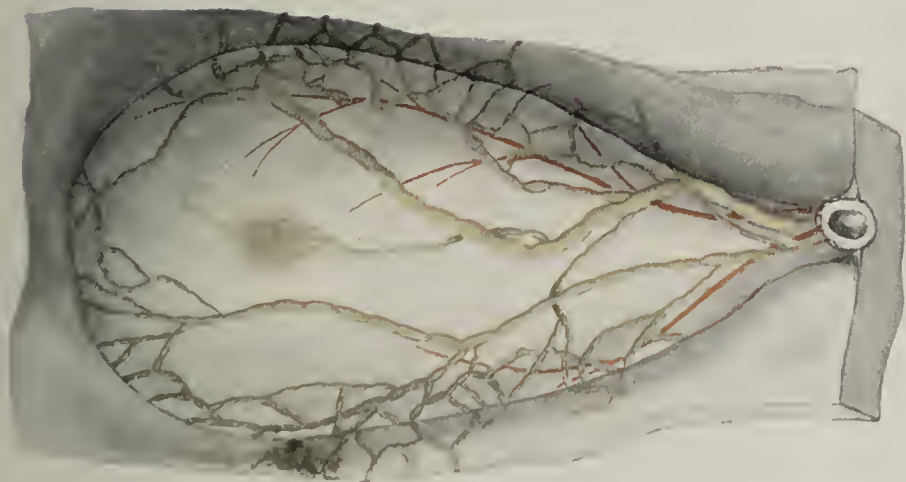


FIG. 1.—Gall-bladder of pig.

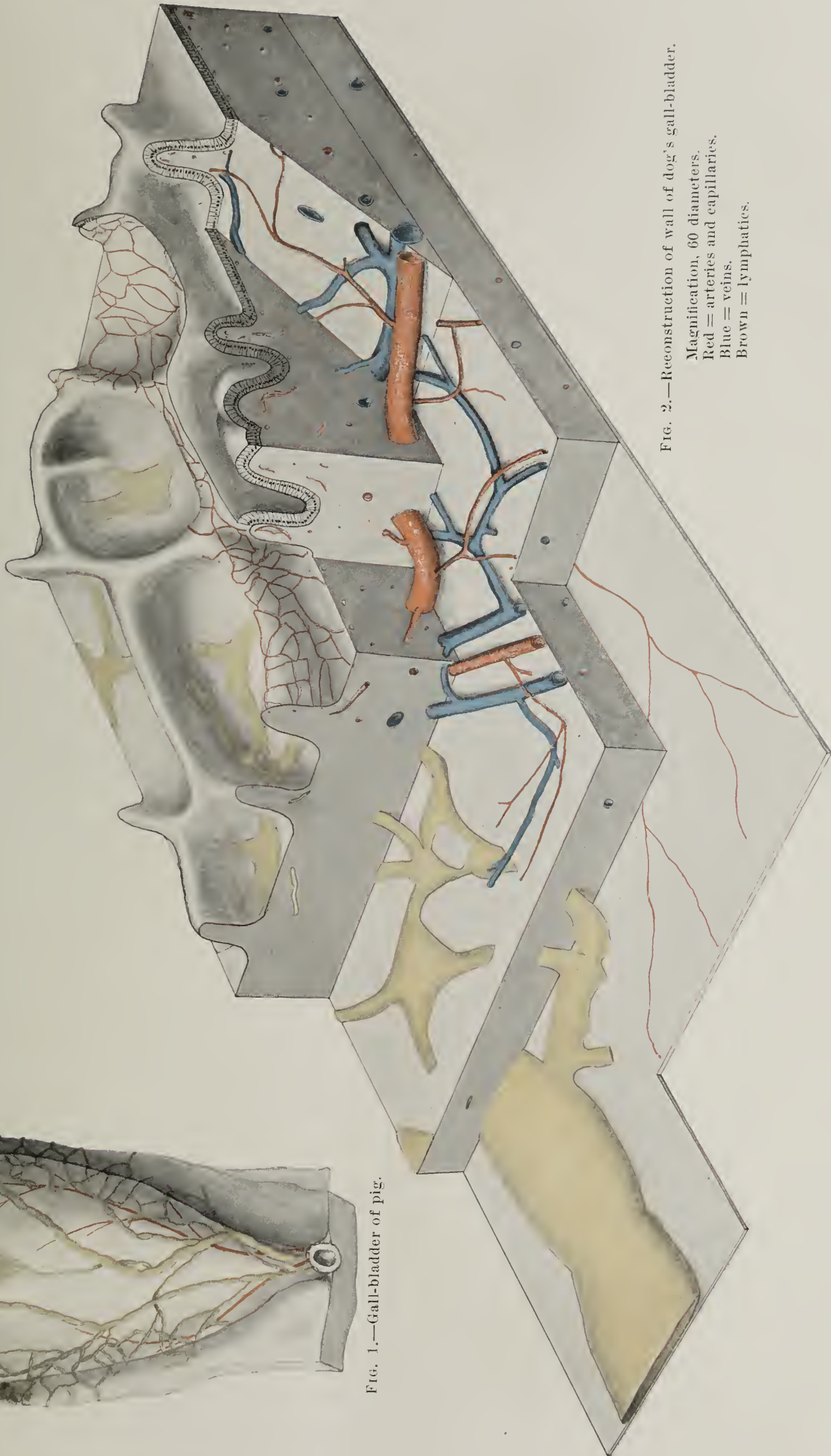


FIG. 2.—Reconstruction of wall of dog's gall-bladder.

Magnification, 60 diameters.
Red = arteries and capillaries.
Blue = veins.
Brown = lymphatics.

M. T. Sudler del.



FIG. 3.



FIG. 4.

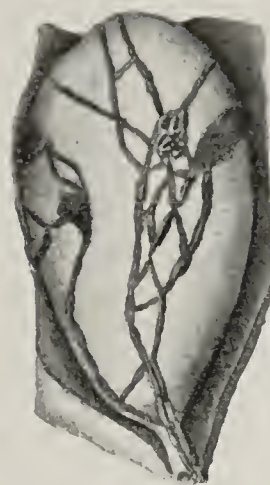


FIG. 5.

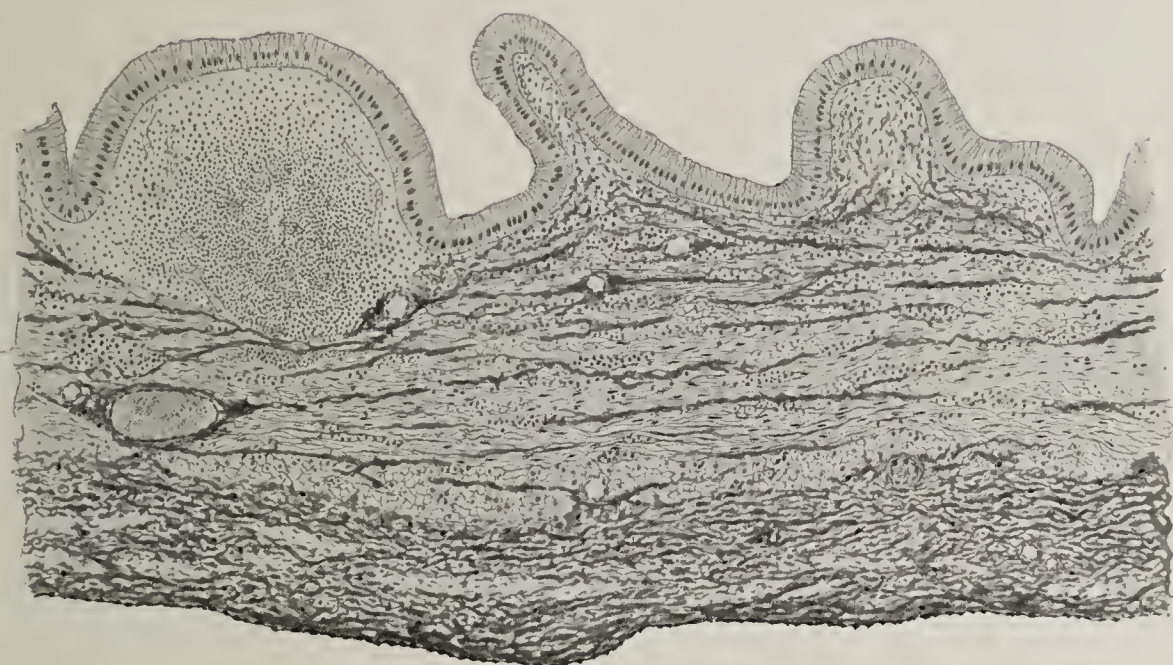


FIG. 6.



FIG. 7.



FIG. 8.

lymphatic vessel coming up from the deeper layer to join the large superficial one. *N* = Needle of syringe.

FIG. 2.—Reconstruction of the wall of the partially contracted gall-bladder of a dog, magnified 60 times, showing the blood-vessels on the right and the lymphatic vessels on the left. Lymph follicles are shown on the right as two rounded eminences just under the epithelium. The vena comites shown is quite characteristic for the larger arteries. The large lymphatic vessel is shown partially collapsed.

FIG. 3.—Gall-bladder of adult man, showing superficial lymphatics. $\frac{1}{2}$ natural size.

FIG. 4.—Gall-bladder of man 19 years old, dead of chronic nephritis, showing the large superficial lymphatics. This gall-bladder gave

evidence of having been through an inflammatory process, and so the lymphatics are probably abnormally numerous.

FIG. 5.—Gall-bladder of dog, showing the superficial lymphatic vessels. Natural size.

FIG. 6.—Section through the contracted gall-bladder of a dog, magnified 80 times, showing the arrangement into coats and the relations of the blood-vessels.

FIG. 7.—The lymphatics of the subserous layer of a dog. (Camera drawing.)

FIG. 8.—The lymphatics of the fibro-muscular layer of a dog, showing their relation to the folds on its surface. These folds are represented narrower and less complicated than in the specimen in order not to hide the lymphatics. (Outlines made with the aid of a camera.)

REMARKABLE CASES OF HEREDITARY ANCHYLOSES, OR ABSENCE OF VARIOUS PHALANGEAL JOINTS, WITH DEFECTS OF THE LITTLE AND RING FINGERS.

BY GEORGE WALKER, M. D.,

Instructor in Surgery, Johns Hopkins University.

Accounts of diverse abnormalities of the arms, forearms, hands, and feet, are to be found in literature from the remotest medical history, and not a few books and monographs on these various defects have appeared from time to time. Most of these reports comprise instances of polydactylism of various degrees; abnormal shapes of the metacarpal and phalangeal bones; absence of the phalanges and carpal bones; increase in the number of the phalanges; absence of fingers; absence of the bones in the arm and forearm; abnormal shapes and lengths of the radius and ulna; lateral union of the phalanges; union of the fingers by the soft parts, etc.

Two cases have recently come to my knowledge which have sufficient bearing on the ones herein reported to warrant a short synopsis of them in this paper.

The first was that of a child in which there was a lateral union of the first and second metacarpal bones of both feet. This was not supposed to be hereditary until the grandmother, upon examining her own foot, to show where the defect had occurred in the child, found her own bones in exactly the same condition. Although she was seventy years old, she had never previously noticed it.

The second case was that of a young girl whom I examined. There was a partial stiffening in the metacarpophalangeal articulation of the thumb; this was ligamentous, and not bony, and permitted a certain amount of motion, probably about one-half that of normal. This defect had occurred in one of her brothers, one uncle, her father and her grandmother. All of them were afflicted in the same joint, and had about the same amount of motion.

The cases which I herewith report show either a complete bony ankylosis or an absence of various joints between the phalanges, together with an absence of one or more bones in the little and ring fingers. As will be seen in the family tree, it has occurred in five generations. I have examined the cases so far as possible, and have made Roentgen photographs from four of them, thus representing two generations. Thomas B. applied to the dispensary of the Johns Hopkins

Hospital for the treatment of leg ulcer. He was fifty-two years of age, well nourished and apparently well developed and healthy. On examination of his hands I found the thumb and index finger normal; in the ring and middle fingers nothing could be seen on inspection in the extended hand, contrary to the usual type, but on palpation there was found an entire bony ankylosis of the second metacarpal joints of above fingers; the bony enlargements corresponding to the heads of the bones were present, and in the middle finger a distinct sulcus could be felt on the thumb side; other than this the enlargement was regular and smooth. The terminal joints were negative. The little finger presented only two phalanges, there being, however, near the end of the first phalanx, a slight enlargement which possibly corresponded to a joint. The thumb was 7 cm. in length; first phalanx, 4 cm.; and second phalanx, 3 cm. The index finger, 8½ cm.; first phalanx, 3¼ cm.; second, 3 cm.; third, 2¼ cm. Middle finger, 9¼ cm.; first and second together, 7½ cm.; third, 1¾ cm. The first from basal joint to middle of enlargement, 4 cm.; the second, from middle of enlargement to distal joint, 3½ cm. Ring finger, 9 cm.; first and second phalanges, 6¾ cm.; third, 2¼ cm. Little finger, 6 cm.; first phalanx, 3½ cm.; second, 2½ cm. The left hand presented nearly the same appearance, and on careful palpation and measurement the only difference found was that in the little finger, first phalanx, there was a slight bowing, making a palmar concavity toward the end. This was due, according to the statement of the patient, to an old fracture. The enlargement at this site, as is shown in Roentgen Photograph No. 1, is very much greater than in the other hand, and suggests that it had probably been caused by trauma; in the other finger the enlargement can be seen, but to a much less degree, thus making it doubtful whether there is an obliterated joint, or the absence of the middle phalanx. The metacarpals were of normal length and their articulations were negative. The carpus was negative. The feet presented nothing abnormal, except a slight giving way of the arch. The other parts of

the osseous system were well developed and did not differ from the usual types. The patient stated that the deformity gave him very little inconvenience, and did not interfere with his work. Both the above hands are shown in Roentgen Photograph No. 1.

On being questioned in regard to his family history, he said that his father, grandfather and great-grandfather were similarly affected. The middle joints of all his father's fingers were stiff; the defect in the grandfather and great-grandfather was known to have existed, but the exact nature could not be determined. He had three uncles and one aunt; two of the uncles he thought were affected, but was not certain; the other uncle and aunt were free. In his immediate family there were four brothers and one sister. One brother and the sister had negative hands; the other three brothers presented the family trait. He had four children, all of whom were free. His younger brother had had three children, two dead and one living, none of whom were affected. His elder brother had eleven children; four of them, two boys and two girls, had the defect. I have visited and examined the two brothers and their families, and I give in the following a report of said examination.

Henry B., the younger brother of the above described, is a gardener, 48 years old; a strong, well built, healthy man; five feet eight inches in height and weighs 148 pounds. Both hands are affected. Right thumb, negative; length, 7 cm.; first phalanx, 4 cm.; second phalanx, 3 cm. Index finger, length, $6\frac{3}{4}$ cm.; first and second, 5 cm.; third, $1\frac{3}{4}$ cm.; the first joint is normal, second is stiff, distinct bony enlargement at site of joint, slight sulcus on thumb side. Middle finger, $9\frac{1}{2}$ cm.; first and second phalanges, $7\frac{1}{2}$ cm.; third, 2 cm.; first from basal joint to middle of enlargement, $4\frac{1}{4}$ cm.; first joint is negative, the second is stiff with rounded, smooth, bony enlargement; no sulci. Ring finger, $8\frac{1}{2}$ cm.; first and second, $6\frac{1}{2}$ cm.; third, 2 cm.; first joint is negative, second ankylosed, bony enlargement not so marked. Little finger, $5\frac{1}{2}$ cm.; first and second, $3\frac{3}{4}$ cm.; third, $1\frac{3}{4}$ cm.; the first joint completely stiff, second negative, metacarpal bones and carpus negative. Other hand presented same appearance and nearly the same measurement. Feet and remainder of bones in the body did not differ from normal.

William B., elder brother, very strong, hale, robust man, 58 years of age, 5 feet 11 inches in height, weighed 172 pounds. Both hands affected, as shown in Roentgen Photograph No. 2. Middle joint, ring and middle finger and both joints in little finger stiff. Thumb and index finger normal, remainder show absence of middle joints. Length of thumb, 7 cm.; first phalanx, $4\frac{1}{2}$ cm.; second phalanx, $2\frac{1}{2}$ cm. Index, 8 cm.; first phalanx, $3\frac{1}{2}$ cm.; second, 3 cm.; and third, $1\frac{1}{2}$ cm. Joints all negative. Middle finger, $9\frac{1}{2}$ cm.; first and second phalanges, $7\frac{1}{2}$ cm.; third, 2 cm. The first joint completely ankylosed, distinct thickening at joint site, with small depression. Ring finger, 9 cm.; first and second, 7 cm.; third, 2 cm.; first joint site presents usual bony enlargement, but no joint was present; second joint negative. Little finger, $5\frac{1}{2}$ cm.; slight palmar concavity, complete ankylosis of both

joints; $1\frac{1}{2}$ cm. from the end there is a slight enlargement with furrow in middle at joint site, but no motion; the first joint is also completely immobile. The metacarpals are normal in length, size and articulation; the carpus is negative. The left hand does not differ in essential characteristics from the one described. The feet presented no abnormality.

The patient stated that he had worked at the same bench with two men for fifteen years, and they had never noticed the defect. He had eleven children in his family, four of whom were affected; the others had perfect hands.

I have seen most of the children of the above described, and the following is the condition of the four who are affected.

Sallie B., aged seventeen, rather poorly developed, tall and slim, height five feet six inches, weight 115 pounds, both hands affected, as shown in Roentgen Photograph No. 3. Thumb and index, free; right hand, thumb, 6 cm.; first phalanx, $3\frac{1}{2}$ cm.; second phalanx, $2\frac{1}{2}$ cm.; joint normal. Index finger, 7 cm.; first phalanx, 3 cm.; second, $2\frac{1}{4}$ cm.; third, $1\frac{3}{4}$ cm.; both joints negative. Middle finger, $8\frac{1}{2}$ cm.; first and second, $6\frac{1}{2}$ cm.; third, 2 cm.; complete ankylosis first joint, second joint is negative. Ring finger is represented only by the first phalanx, which is 4 cm. in length. The distal end is slightly enlarged, and tapers towards middle finger. The little finger is represented also by only first phalanx, $3\frac{1}{2}$ cm. in length. It presents same shape of enlargement at distal end as ring finger. The left hand is the same as right, except that the middle joint of the index finger is ankylosed. In these hands, notably in the left one, there is a distinct crowding together of the metacarpals, being most marked in the fifth, which, as shown in the photograph, decidedly overlaps the fourth. The carpi are negative; the remainder of bones apparently normal. The feet were not examined, but according to the statement of the patient they presented no abnormalities.

Carrie B., aged fifteen, rather strong and robust, weight one hundred and seventeen, five feet four inches in height. I was unable to procure a photograph of this hand on account of the unwillingness of the patient. Both hands are affected, and very similar to those of her sister, as above described. Right hand, thumb and index finger, normal. Ring and little fingers of both hands, as in the case of her sister, present only one phalanx, that of the ring finger is 4 cm. in length, and that of the little, 3 cm.; the distal ends are slightly enlarged, and according to palpation are like her sister's. In the other hand the index finger is ankylosed at the middle joint, and the middle finger presents a striking peculiarity in that the ankylosis is in the second joint, the first being free.

Henry B., a picture of whose hand I was unable to obtain, but upon examination found the following conditions:

Not very robust, tall and slim, age fifteen; height five feet six inches, weight one hundred and twenty pounds, both hands affected. Index and thumb in both negative, remainder affected. Thumb, right, $5\frac{1}{2}$ cm.; first phalanx, 3 cm.; second phalanx, $2\frac{1}{2}$ cm.; joint negative. Index, $7\frac{1}{2}$ cm.; first phalanx, 3 cm.; second, $2\frac{1}{2}$ cm.; third, 2 cm.; phalanges normal in size, and joints negative. Middle finger, $8\frac{1}{2}$ cm.; first and second

phalanges, $6\frac{1}{4}$ cm.; third, $2\frac{1}{4}$ cm.; first joint is stiff with distinct bony enlargement, and slight depression between heads of bones; second joint is negative. Ring finger, 8 cm.; first and second, 6 cm.; third, 2 cm.; first joint is ankylosed, second is negative. Little finger, $5\frac{1}{2}$ cm.; first phalanx, 4 cm.; middle is absent; the third, $1\frac{1}{2}$ cm. There seems to be an entire absence of the second phalanx; the first is normal and presents no enlargement which might correspond to a joint. The left hand differs in one particular from the above described, in that the terminal phalanx of the little finger is turned inward toward the ring finger, and forms an angle of 135 degrees with the second phalanx. The metacarpals and carpi are negative. The remainder of the bones present no defects.

George B., aged seventeen, height five feet six inches, weight one hundred and fifteen pounds, rather poorly developed, slightly anemic. Both hands shown in Roentgen Photograph No. 4. Right hand, thumb, 6 cm.; first phalanx, $3\frac{3}{4}$ cm.; second, $2\frac{1}{4}$ cm., joint, normal. Index finger, 7 cm.; first and second, $4\frac{3}{4}$ cm.; third, $2\frac{1}{4}$ cm.; first joint site shows normal enlargement, but is stiff; second is negative. Middle finger, 8 cm.; first and second, 6 cm.; third, 2 cm.; first joint completely ankylosed; second, negative. Ring finger, $7\frac{1}{2}$ cm.; first and second, $5\frac{1}{2}$ cm.; third, 2 cm.; first joint stiff; second, negative. Very slight enlargement at first joint site. Little finger, 5 cm.; first, $3\frac{1}{4}$ cm.; second, absent; third, $1\frac{3}{4}$ cm. Joint is negative; first phalanx is normal in length and shape, there being no enlargement nor anything to suggest an ankylosed joint. Metacarpals and carpi negative. The other hand presented the same appearance. The remainder of the body negative.

In perusing the literature bearing on these subjects, I have found only a few similar cases reported, none of them being so marked as mine, and only one was hereditary.

Klausner, in a rather exhaustive monograph on various deformities of the arm and hand, reports a case in which the ankylosis was present in the second phalangeal joint of the index finger; the hand was very much deformed otherwise, and the fingers partly webbed. There was no hereditary history, nor were any other members of the family so affected.

Wolf, very recently, has put on record an ankylosis of the second phalangeal joint of the little finger. In this case the middle phalanx was very much shortened and was joined to the first by a bony union at an angle of about 145 degrees. The terminal phalanx was apparently normal. This ankylosis had occurred in four generations, and was present in eight instances. Some of them were inherited from the father and others from the mother. The same joint of the same finger was affected in every case; the remainder of the hand was normal; there is no record of any other defects in the body; the condition of the pectoral muscles is not mentioned. The fingers in the cases of both Klausner and Wolf are shown by Roentgen photographs.

R. Stintzing reports a case of a very much deformed hand in which there was an almost complete ankylosis in the second joint and partial in the first. In this case the fingers

were webbed; a diminution in the length of several of the middle phalanges and a defect in the right pectoralis major muscle.

J. Sklovowski relates an instance of a defect of the sternum, pectoralis major and minor muscles, and a portion of the back muscles, together with an absence of the second phalanx in the second and third fingers; a shortening of the other phalanges, and a limitation of movement in nearly all of the phalangeal joints, with a complete ankylosis of both joints in the fourth finger.

Hoffman describes a deformity occurring in a man 48 years of age, in which there was a stiffening in one or more phalangeal joints, and a shortening of the middle phalanx of the middle finger. In the index finger the middle phalanx was small and completely fused with the third phalanx. There was also webbing of the fingers, associated with muscular defects in the chest and back muscles.

Fuerst gives an accurate account of a hand which was examined after death by a very careful dissection. In this hand there was great shortening and malformation of the middle phalanx of the middle and ring fingers. There was no ankylosis in any. In all of the above cases, with the exception of the last, the observations have been made on the living subject, and usually by palpation alone.

With the exception of the two girls in the present generation of the cases which I herewith report, none of the females have heretofore been affected, and in them appeared the only instances in which the terminal phalanges were absent. There is another striking difference in one of them, as is shown in the Roentgen Photograph No. 2, in the partial overlapping of the fifth metacarpal bone, which suggests the possibility that continued transmission might produce a fusion, or an absence of one of these bones.

From the above it will be seen that the defects have existed in five generations, and have been confined entirely to the hands, the remaining osseous system presenting no peculiarities. Except in the present generation the hands have been otherwise normal. The first departure from this was in the case of the boy, Roentgen Photograph No. 4, where there is an absence of the middle phalanx of the little finger; while in both of the girls, as is shown in one by the Roentgen Photograph No. 3, the end and the middle phalanges of the middle and ring fingers are absent. There is also a partial obliteration of the distal enlargement of the remaining phalanges.

By a study of the photographs, one can see that there is undoubtedly a bony union and not a fibrous ankylosis in the joint sites. The enlargements corresponding to the heads of the bones are plainly to be seen and felt, but the joints are absolutely unformed. In a number, small sulci could be palpated, corresponding to the normal depression between the heads of the bones. The photographs also show that there is a certain porosity at the joint sites, which seems to be more than normal.

The question arises whether these are cases of entire absence of the joints, or of early ankylosis. The two phalanges are about the normal length, and there is a distinct enlarge-

ment corresponding to the metacarpal heads, with small sulci between some of them, but other than this there is no evidence whatever of an attempted joint formation. In view of the fact of a complete bony union, it appears best to consider them as cases of an absence of the joint rather than of an ankylosis. It has been suggested that probably the ankylosis may have occurred after birth as the result of some disease; but according to the statements of the mothers of these various children, it was a congenital defect. A careful examination of the other bones failed to show any abnormal conditions or diseases, and the history of lues was not present.

The examination of the arm shows a fairly good muscular development, and so far as could be made out there was no atrophy of the flexor sublimis digitorum. The muscles of the hand were also well developed and the thenar and the hypothenar eminences were apparently normal. There was an exception to this in the hand of the girls, where there was found a rather poor development of the hand muscles, which was most notably marked at the hypothenar eminence.

The palmar folds in the hand were normal, but in the skin over the ankylosed joints they had become nearly smoothed out; the two normal creasings being scarcely discernible.

The epiphyses were all joined; which was unfortunate as otherwise some light might have been thrown on the bony development.

In nearly all of the reported cases there have been defects in the back and breast muscles; the most striking examples of which were found in the pectoral region. The cases which I herewith report presented no such abnormality, and showed upon examination a completely developed condition of the muscles of the arm, shoulder and back. In all the instances the feet were negative.

These cases are in striking contrast to the generally accepted opinion that deformities of the hands and feet are transmitted by the mother, for in each of those in this series it came through the father, the mothers having all been normal. It is most interesting to note that in each generation only one male member has transmitted the deformity to his offspring.

The occupations of the individuals were very little interfered with; the only inability complained of was that of being unable to grasp small articles with the whole hand. The deformity, except in the cases of the two girls, was not at all striking, and unless one carefully inspected the hands it would be overlooked, and even in shaking hands it was not noticeable.

SHORTENING OF THE PHALANGES.

In my cases, as well as in most of the above-reported ones, there has been a decided shortening of one or more of the phalanges. It has been in nearly every instance most strikingly observed in the middle phalanx with a certain predilection for the little finger.

In discussing such cases, Fuerst states that in nearly all of these defects the shortening is seen in the middle phalanx, and he ascribes it to the fact that in embryologic development the middle phalanx is the last to become bony. This

occurs when the embryo is about 8 centimeters in length, and he thinks that at this period the deformity commences. From observations of his case, and a study of certain others, he concludes that the shortening and ankylosis are stages in fusion of the first and second bones. The shortening represents the first stage; the ankylosis the second stage, and the whole phalanx the third stage.

This theory does not seem to be based upon sufficient observation, nor is there enough evidence in the studied cases to justify any such assumption.

In my cases, as is shown in the photographs, there is no shortening at all in the phalanges of the second and third fingers, although a complete ankylosis exists; this would stand directly against the theory which Fuerst has advanced. In the little finger, however, there is some evidence for the hypothesis, for in the second generation there is present a diminution in the phalanx, then an ankylosis, and finally, in the case of the boy, the joint has entirely disappeared, and there remain only two normal phalanges.

A very distinct and decidedly unique type, so far as the above-mentioned cases are concerned, is to be seen in the hand of the girl; for in this case the end and middle phalanges have entirely disappeared, and have left the first phalanx only partially developed. The diminution and absence of the end phalanx were not noted in the other reported cases, and can not be explained on the ground of the late bony development.

The little finger first shows a beginning defect, and in the case of Thomas B., Roentgen Photograph No. 1, left hand, the first phalanx is long, somewhat curved, and presents a slight enlargement which probably corresponds to a joint site. The middle phalanx then will be represented by a small bone about $1\frac{1}{2}$ cm. in length. In the case of the nephew there are certainly only two phalanges; and in each of the girls only one is present, and the defect has extended to the ring finger.

Thanks are due to Dr. Finney for permission to report these cases. I am also indebted to Professor W. A. S. Hammel for the care which he gave to the preparation of the photographs.

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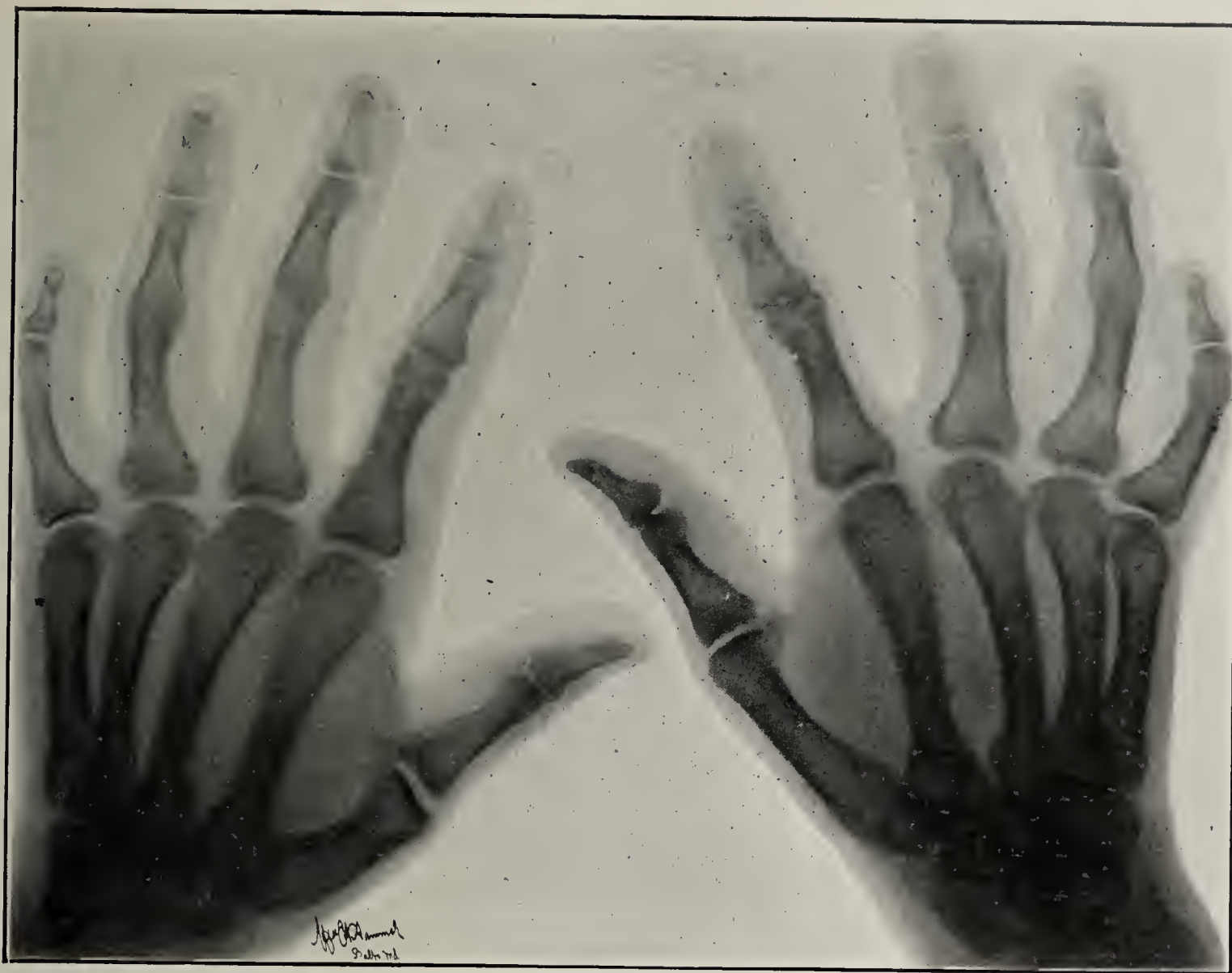


FIG. 1.



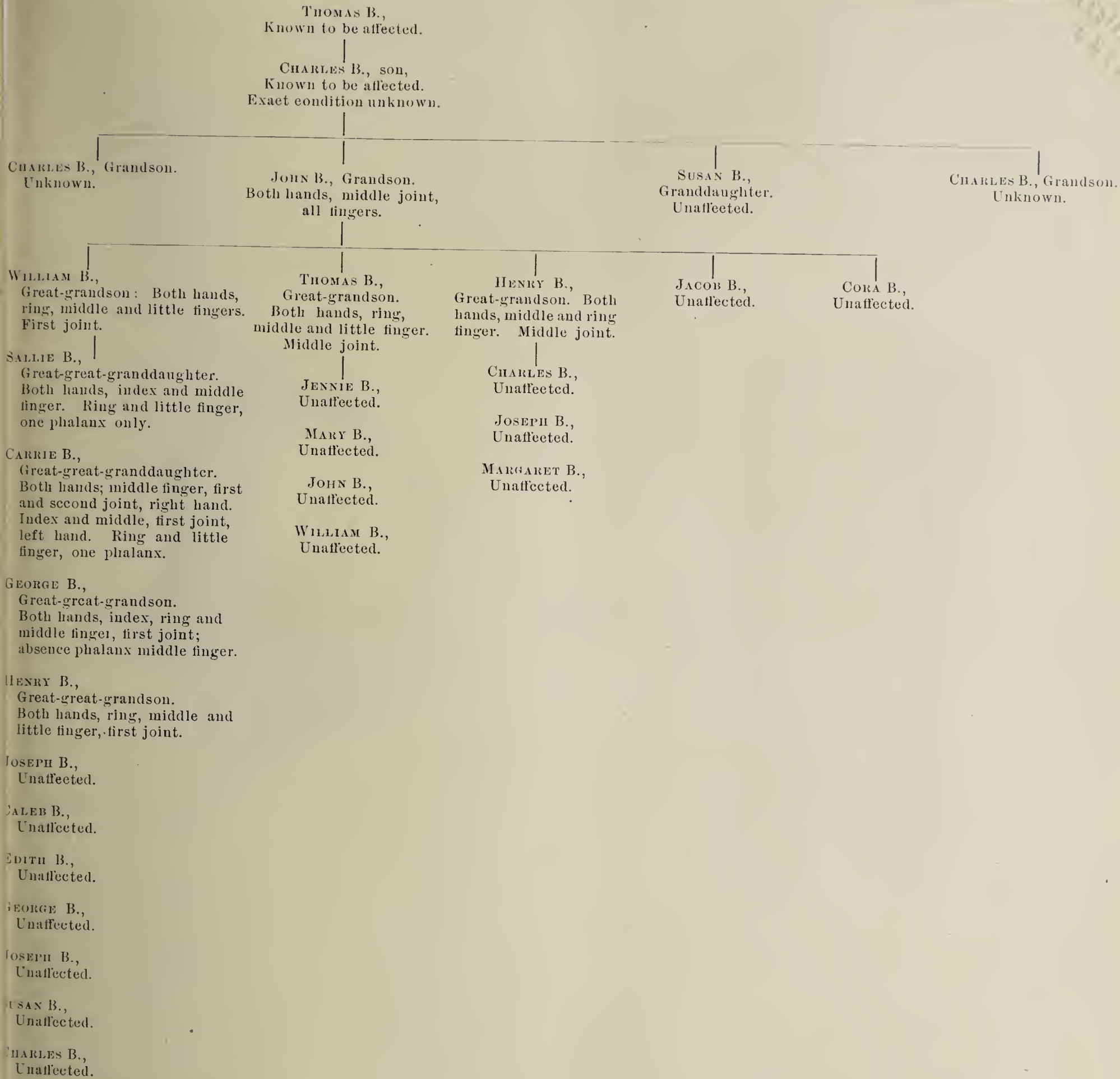
FIG. 2.



FIG. 3.



FIG. 4.



NOTE ON THE BASEMENT MEMBRANES OF THE TUBULES OF THE KIDNEY.

BY FRANKLIN P. MALL.

Professor of Anatomy, Johns Hopkins University.

In an earlier publication upon reticulated tissues in general the statement was made that the whole framework of the kidney, including the basement membranes, from the capsule to the pelvis, is formed by one mass of anastomosing fibrils, and that the sharp borders of the fibrils mark the outlines

of the tubules to form the basement membranes which in ordinary sections appear to be homogeneous.¹ This statement was based upon observations made by digesting frozen

¹ Mall, Abhandl. der math.-phys. classe der Königl. Säch. Gesell. der wissensch., Bd. 16, and Johns Hopkins Hospital Reports, vol. 1.

sections of the kidney, digested in pancreatin, stained with acid fuchsin and differentiated with picric acid. By this method all of the cells and other structures of the kidney are destroyed, leaving only the white fibres and reticulated fibrils which are stained intensely red. This observation has been confirmed by Rühle,² who used a method similar to the one I employed. Rühle digested small blocks of kidney (after hardening in alcohol) with pancreatin until all the cells were dissolved, then made sections in paraffin, which were stained upon the slide. By this method the topography of the reticulum is retained much better than is the case in specimens made by the freezing method.



FIG. 1.—Longitudinal section of the framework encircling a kidney tubule digested in pancreatin, stained with acid fuchsin, and differentiated with picric acid. Enlarged 333 times.

The work of Rühle, which is very accurate and extensive, shows quite conclusively that the fibrils obtained by his method, as well as by the freezing method, are identical with those which form the interstitial tissue as seen in ordinary sections.

The observations given above have been confirmed by Disse,³ who states, however, that the basement membranes of the kidney which have been isolated by means of strong acids always appear to be homogeneous. This he explains by assuming that pancreatic digestion resolves the membrane into fibrils by dissolving the cement substance between them. The strong acids, however, dissolve the interstitial connective

tissue but do not affect those fibrils which are stuck together by the cement substance to form basement membranes.

Von Ebner⁴ is of the opinion that the fibrillar appearance of the basement membranes of the kidney is due to fine folds in it owing to the method of preparation. He further states that the fibrils of connective tissue between the tubules stain with acid fuchsin while the membranes do not. There is some truth in this statement, for in sections of the kidney which have been macerated and slightly tinged the stained fibres shine through the homogeneous membrane, often making it appear folded. Yet with some care the true nature of these makings is easily determined.

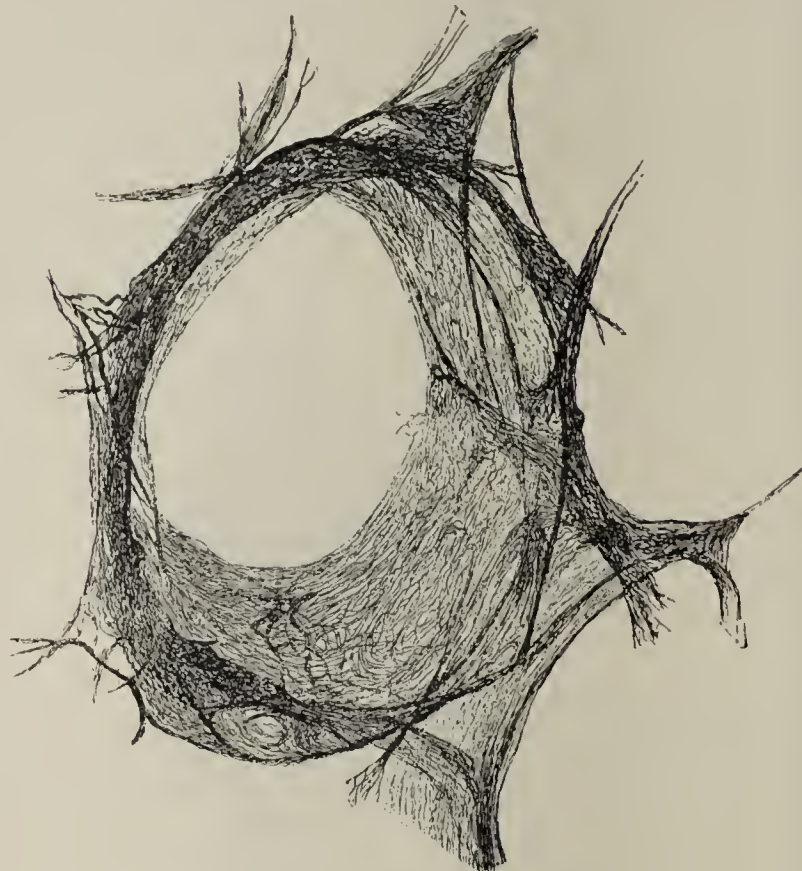


FIG. 2.—Transverse section of the reticulum encircling a kidney tubule prepared as Fig. 1.

Recently, while studying sections of the fresh kidney by means of various methods, I obtained specimens which proved that the observations of Rühle, Disse and myself are correct, so far as they go, but that our conclusions regarding the basement membranes are not correct. The baskets, which I reproduce in Figs. 1 and 2, do exist, are easily obtained by means of pancreatic digestion, but do not form the basement membranes. An additional membrane, the basement membrane, lies within this tube and is totally destroyed by means of pancreatic digestion. The most instructive specimens I obtained were made by macerating frozen sections of the rabbit's kidney in a cold saturated solution of bicarbonate of soda for a number of days, after which most of the cells have been converted into a slimy mass. Shaking the section vigorously in water soon cleared the framework, which was next spread upon a slide and examined. In case most of the cell remnants had been removed the section was dried upon the slide, stained with acid fuchsin, differentiated with picric

² Rühle, *Hist. Archiv*, 1897.

³ Disse, *Sitzungsberichte der Gesellsch. zur Beförderung der gesamten Naturwissenschaften zu Marburg*, November, 1898.

⁴ Von Ebner, *Kölliker's Handbuch der Gewebelehre*, Bd. 3, S. 374-375.

acid and mounted in balsam. Successful sections prepared in this way show the basement membranes partly filled with the remnants of epithelial cells, the interstitial reticulated connective tissue and the blood-vessels. A portion of such a specimen is shown in Fig. 3.

After specimens of the basement membranes and the reticulum are obtained through maceration in bicarbonate of soda, as described above, they may be treated with various reagents to test their properties. Dilute solutions of HCl and KOH cause the reticulum to swell and become transparent, while the basement membrane and the elastic fibrils accompanying the arteries remain unchanged. But it is shown by the Weigert's elastic tissue stain that the membranes are not elastic, for they do not take on the stain while the elastic tissue fibres do. Furthermore, Mallory's connective tissue stain,⁵ stains the reticulum but not the membranes. As far as I have tested the basement membranes they give reactions

⁵ Mallory, *Journal of Experimental Medicine*, vol. 5.

much like the membranes of elastic fibres, but whether they are identical with them I have been unable to determine.



FIG. 3.—Longitudinal section of a kidney tubule with the surrounding reticulum from a specimen macerated in bicarbonate of soda for a week, shaken, dried upon the slide, stained with acid fuchsin and differentiated with pierie acid. The basement membrane partly filled with broken epithelial cells and surrounded with reticulum are shown. The drawing is semidiagrammatic.

A COMPARATIVE STUDY OF THE DEVELOPMENT OF THE GENERATIVE TRACT IN TERMITES.¹

By H. McE. KNOVER, PH. D.,

Instructor in Anatomy, Johns Hopkins University.

The facts here presented furnish a more accurate guide in estimating the status of individuals in the community than has been hitherto available. New light is thrown on hypotheses as to the possible influence of workers and soldiers in the transmission of hereditary characters in these communities. These studies will also be seen to bear on problems of the comparative morphology of the sexual organs of insects. Six species of two genera (*Calotermes* and *Termes*) were investigated.

The efferent passages and accessory glands of Termites are simple, as in *Thysanura*. In *Termes flavipes* they arise first in larvæ just hatched, in which the mesodermic duct from ovary or testis ends blindly against the ectoderm of the hypodermis. In the female three separate and segmental, unpaired invaginations of the ectoderm appear, one behind another on the ventral mid-line. The pouch of the anterior segment comes into contact with the mesodermic oviducts, that of the next segment later becomes the receptaculum seminis, while the posterior invagination bifurcates at its inner end and eventually forms the colleterial glands. In larvæ preceding those evidently destined to become workers and soldiers, and in adult workers and soldiers, this disconnected segmental condition persists (Fig. 1). In other words, the workers and soldiers exhibit a peculiar arrested,

larval stage in the development of the sexual apparatus. In older larvæ of sexual individuals the three, segmental, independent rudiments telescope together and unite to form a vaginal canal with colleterial glands, receptaculum seminis, and mesodermic oviducts opening into it. In the male there

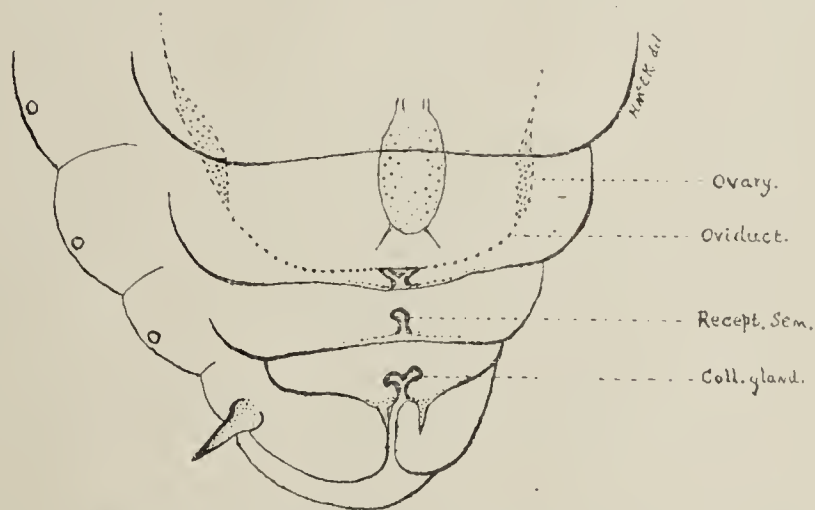


FIG. 1.—Modified camera sketch of ventral aspect of tip of abdomen of *Termes flavipes*, adult worker or soldier. Female.

is a single median ectodermic invagination into which the paired, mesodermic vesiculæ seminales, and vasa deferentia, eventually open (Fig. 2). In adult workers and soldiers of this sex an arrested larval type is exhibited in the sexual apparatus.

Modifications of this history occur in other species, affecting workers and soldiers especially.

¹ A preliminary abstract presented to the American Morphological Society, December, 1900.

In a species of *Eutermes* from Jamaica the most extreme modification is found. Not even rudiments of the ectodermic passage and accessory glands appear in workers or soldiers (Nasuti) of this species. The origin of the ectodermic apparatus of sexual individuals of this species is, however, essentially that of the corresponding structures of *flavipes*.

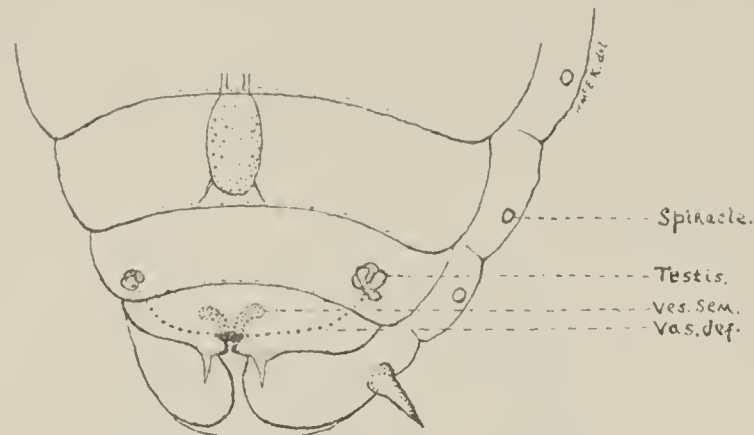


FIG. 2.—Similar sketch of adult worker or soldier. Male.

The condition of the mesodermic sexual gonads, male and female, is very simple in a Jamaican species of *Calotermes*, a primitive genus of the group. In advanced larvæ and in soldiers the ovary is a series of egg-tubes opening into the

oviducts, while the testis is composed of the same number of tubules or follicles arranged serially on the vas deferens.

In *T. flavipes* and in the Jamaican *Eutermes* the youngest larvæ exhibit a condition similar to that in *Calotermes*, which arrangement, it will be observed, bears a suggestive resemblance to the type found in *Thysanura*.

In the Jamaican *Eutermes* the workers and soldiers exhibit an extreme arrest of the development of the gonads, which do not proceed beyond the stage found in the youngest larva just hatched.

The adult workers and soldiers of a Japanese species of *Termes*, unlike *T. flavipes*, possess gonads not greatly modified from the serial type which seems to be primitive.

In *T. flavipes* the gonads of older larvæ and of adult workers and soldiers in both sexes lose this primitive type; the tubules of the testicle, for instance, becoming twisted into a globular mass in which the original serial order is obscured.

The gonads of larvæ of sexual individuals, in all species studied, change from the condition at hatching to a type in which the simpler original arrangement is much obscured.

Additional facts with suitable discussions will be published shortly, fully illustrated.

A COMPOSITE STUDY OF THE AXILLARY ARTERY IN MAN.

By J. M. HITZROT.

(From the Anatomical Laboratory of the Johns Hopkins University.)

At the suggestion of Dr. Mall the following records were made from dissections in the Anatomical Laboratory of the Johns Hopkins University during 1898-99 and 1899-1900. Charts¹ were furnished the students with the request that they draw the axillary artery with its branches, etc., as found in their subjects, giving as nearly as possible the origin and distribution of each branch and maintaining the relation to the pectoralis minor and the various bony structures of the axillary region. The charts were merely outlines of the skeleton upon which each student sketched his dissection. When this sketch was finished it was added to or changed by the writer, so that the sketch might, as nearly as possible, represent the artery as it existed in each dissection. Parallel with these drawings a set of notes was kept in which the constant and the unusual branches of the artery were carefully noted. During the year 1898-99, considerable difficulty was experienced with the terms short thoracic, acromio-thoracic, etc., the student in his eagerness to apply these terms to the different branches often overlooking the more important feature, *i. e.*, the distribution of the branch. To obviate this to some extent the charts of this year were compiled and the composite picture thus obtained was drawn and furnished as a guide for the future. The terms before mentioned were kept but special stress was laid upon the origin and distribu-

tion of the artery. The results thus obtained were uniformly more satisfactory than those of the previous year.

The charts used in the following tabulations are less than a third of the total number made. The remainder, because of errors in drawing, broken arteries in dissecting, and discrepancies between the notes of the writer and the sketches, were omitted. These omitted charts, in so far as they were of any value, gave practically the same results as were obtained from the tabulation of the correct and more complete charts. In making the tabulations the arbitrary divisions given by the various anatomists were used.

Part I, that portion of the artery extending from the lower border of the first rib to the upper border of the pectoralis minor.

Part II, that portion of the artery which is beneath the pectoralis minor.

Part III, that portion of the artery which extends from the lower border of the pectoralis minor to the lower border of the tendons of the *teres major* and *latissimus dorsi*.

During the first tabulation separate tables were made for the right and left sides to determine whether the origin and distribution differed on the two sides. As the only difference found was in the presence or absence of the long thoracic artery this distinction was dropped, the relative difference consisting in the more constant presence of the long thoracic artery on the left side.

¹ Bardeen, Outline Record Charts used in the Anatomical Laboratory of the Johns Hopkins University, Johns Hopkins Press, Baltimore, 1900.

The charts themselves conveniently fall into different types, that is, the artery in a certain number of instances gives off its branches from the same divisions of the arterial trunk and these branches are distributed to the same regions. The 47 charts here tabulated fall into 7 types, type I being present in 20 cases; type II in 9 cases; type III in 7 cases; type IV in 4 cases; type V in 3 cases; and types VI, VII each in 2 cases.

TYPE I (FIG. 1 AND TABLE I).

This type, the most constant found in the laboratory during the two years the dissections were observed, differs from the text-book descriptions by the absence of the long thoracic artery. The area ordinarily supplied by this artery, accord-

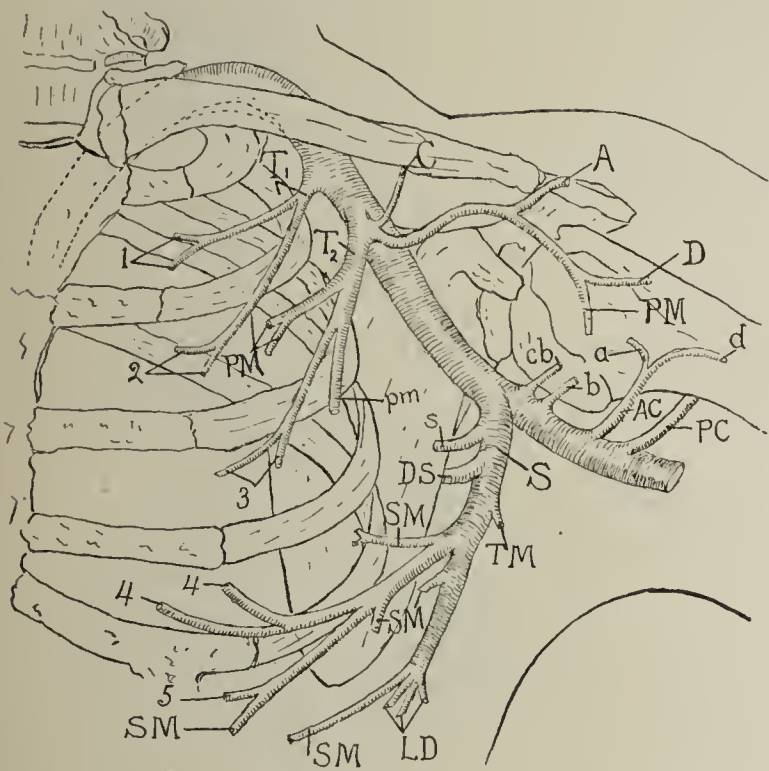


FIG. 1.—Type I of the axillary artery. Present 20 times in 47 cases.

A, Ramus acromialis; a, Ramus ascendens; AC, A. circumflexa humeri anterior; b, M. biceps; C, R. claviculae; cb, M. coraco-brachialis; D, M. deltoideus; d, Ramus anastomoticus; DS, A. circumflexa scapulae, (dorsal scapular); LD, M. latissimus dorsi; P, R. pectoralis; PC, A. circumflexa humeri posterioris; PM, M. pectoralis major; pm, M. pectoralis minor; S, A. subscapularis; s, M. subscapularis; SM, M. Serratus anterior (magnus); SP, A. profunda brachii, (superior profunda); T¹, A. thoracalis suprema; T², A. thoraco-acromialis; T³, A. thoracalis lateralis; TM, M. teres major; 1, 2, 3, 4, 5, 1st, 2d, 3d, 4th and 5th intercostal spaces.

ing to text-books, being supplied by branches from the acromio-thoracic and subscapular arteries. The branches in this type can be conveniently arranged in the following schema:

Part I.	{	1. Superior thoracic.	{	1. Thoracic branch.
		2. Acromio-thoracic.		2. Acromio-humeral branch.
Part II.	{	No branches.	{	3. Clavicular.
Part III.	{	1. Subscapular.	{	1. Dorsal scapular.
				2. Muscular branches.
				3. Anterior.
				4. Posterior.
	{	2. Anterior circumflex.	{	Ascending branch.
				Anastomotie.
		3. Posterior circumflex.		Muscular.
				Anastomotie.
	{	4. Muscular branches.	{	Coraco-brachialis.
				Biceps.

The superior thoracic (A. thoracalis suprema) rises just below subclavius muscle and crosses the first interspace, ending in it and in the second interspace. The origin of the artery is remarkably constant in this type (19 times in 20 cases), it supplies the muscles in the first and second interspaces.

The acromio-thoracic (A. thoraco-acromialis) rises from Part I, about midway between the clavicle and upper border of the pectoralis minor, runs almost directly anteriorly and divides into the (1) thoracic branch, (2) the acromio-humeral and (3) clavicular branch.

This artery is the most constant in this type, being present in all 20 cases. The thoracic branch turns downward beneath the pectoralis minor, giving off branch to the pectoralis major and minor, and to the second and third intercostal spaces and the overlying skin. The acromio-humeral branch runs upward and outward across the costo-coracoid membrane over the coracoid process of the scapula and gives a branch to the acromion and accompanying the cephalic vein between the deltoid and pectoralis major breaks into branches, supplying these two muscles and the surrounding fascia and skin. The clavicular branch is a small branch which turns upward to supply the subclavius muscle.

The subscapular artery arises from the axillary trunk at the lower border of the subscapularis muscle and takes a downward and inward course through the axilla. Near its origin it gives off a branch to the subscapular muscle and a large branch, the dorsal scapular, which passes through the triangular space formed by the subscapularis, teres major and long head of the triceps, to the dorsum of the scapula, supplying the muscles of that region. A small branch to the teres major muscle then comes from the subscapular trunk as it crosses that muscle, and before it splits into the thoracic or anterior branch and its posterior or muscular branch. The thoracic branch crosses the base of the axilla from the back to the front and supplies the serratus magnus, the fourth and fifth interspaces, and the adjacent skin. The posterior branch continues the downward and backward course of the subscapular trunk to end in the serratus magnus, and the latissimus dorsi, giving off numerous branches to these muscles.

Two small muscle branches are given off to the coraco-brachialis and biceps.

From the anterior portion of the axillary trunk a small artery, the anterior circumflex, rises, passes beneath the coraco-brachialis and biceps and sends a branch to the joint by way of the bicipital groove and a branch around the arm to anastomose with the posterior circumflex artery. In its course it gives off branches to the overlying muscles. At about the same level and from the posterior portion of the axillary artery the posterior circumflex takes its origin, passes downward and backward through the space bounded by the teres minor, long head of the triceps, teres major and the humerus, winds around the neck of the humerus, supplying the deltoid, the joint, the triceps, and the adjacent skin

and anastomoses with the anterior circumflex artery and superior profunda artery.

TYPE II (FIG. 2 AND TABLE II).

The branches in type II are conveniently arranged according to the following plan:

Part I.	Superior thoracic.	<ol style="list-style-type: none"> 1. Thoracic branch. 2. Acromio-humeral branch. 3. Clavicular branch.
	Acromio-thoracic.	
Part II.	Long thoracic.	
Part III.	Subscapular.	<ol style="list-style-type: none"> 1. Dorsal scapular. 2. Muscular branches.
		3. Posterior branch.
	Trunk.	<ol style="list-style-type: none"> Anterior circumflex. Posterior circumflex.

This type differs from type I only by the presence of a branch from the part II of the axillary trunk and corresponds

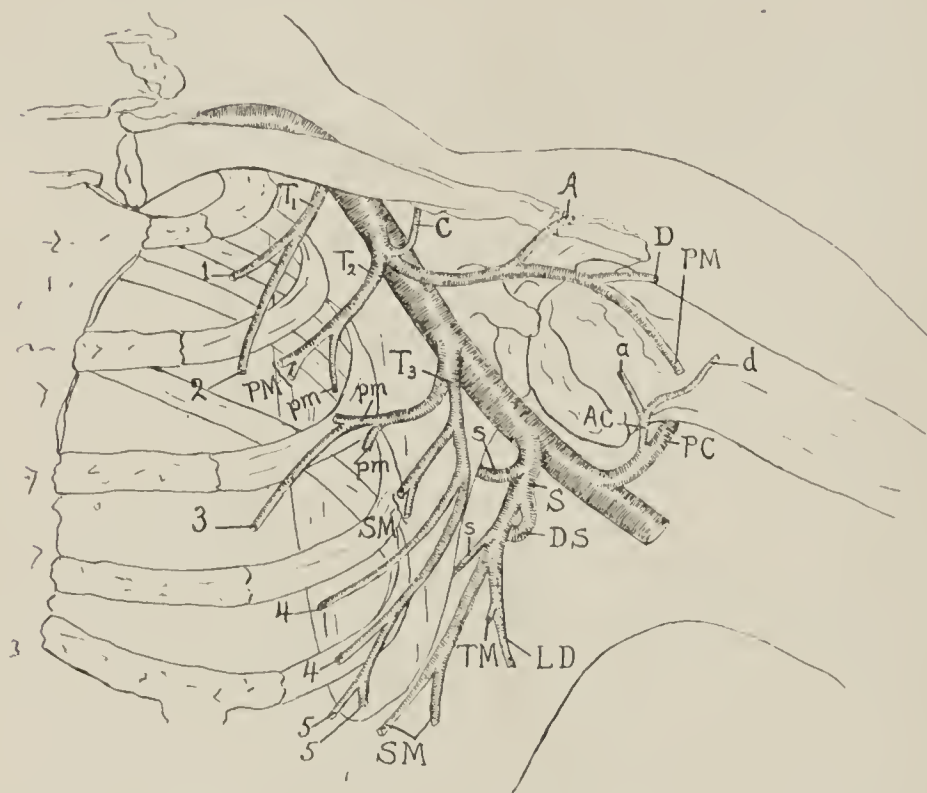


FIG. 2.—Type II of the axillary artery. Present 9 times in 47 cases.

with the description of the axillary artery usually given in the text-books. This branch from the second part of the artery bears the name long thoracic (*A. thoracalis lateralis*). It takes its origin beneath the pectoralis minor, courses downward along the lower border of this muscle, supplying it, the serratus magnus, and the third, fourth and fifth interspaces. In its course it gives off small branches to the fascia of the axilla, and terminal branches which piercing the pectoralis major terminate in the overlying skin. The other arterial branches have the same origin and distribution as described in type I, except that the intercostal areas of the thoracic branch of the acromio-thoracic artery and the thoracic branch of the subscapular artery are replaced wholly or in part by this branch from part II. The anterior and posterior circumflex arteries arise by a common trunk but otherwise their course and distribution correspond to the description given under type I.

TYPE III (FIG. 3 AND TABLE III).

Part I.	Superior thoracic	<ol style="list-style-type: none"> 1. Thoracic branch. 2. Muscular branches. 3. Posterior circumflex. 4. Dorsales scapulae. 5. Anterior branch. 6. Posterior "
	Acromio-thoracic.	
Part II.	Subscapular.	
Part III.	Anterior circumflex.	Ascending.
		Anastomotic.

The branches from part I are similar in their origin and distribution to those described in type I. From part II a large subscapular artery takes its origin. It immediately gives off a branch (thoracic) which supplies the serratus magnus and crossing the axilla beneath the pectoralis minor

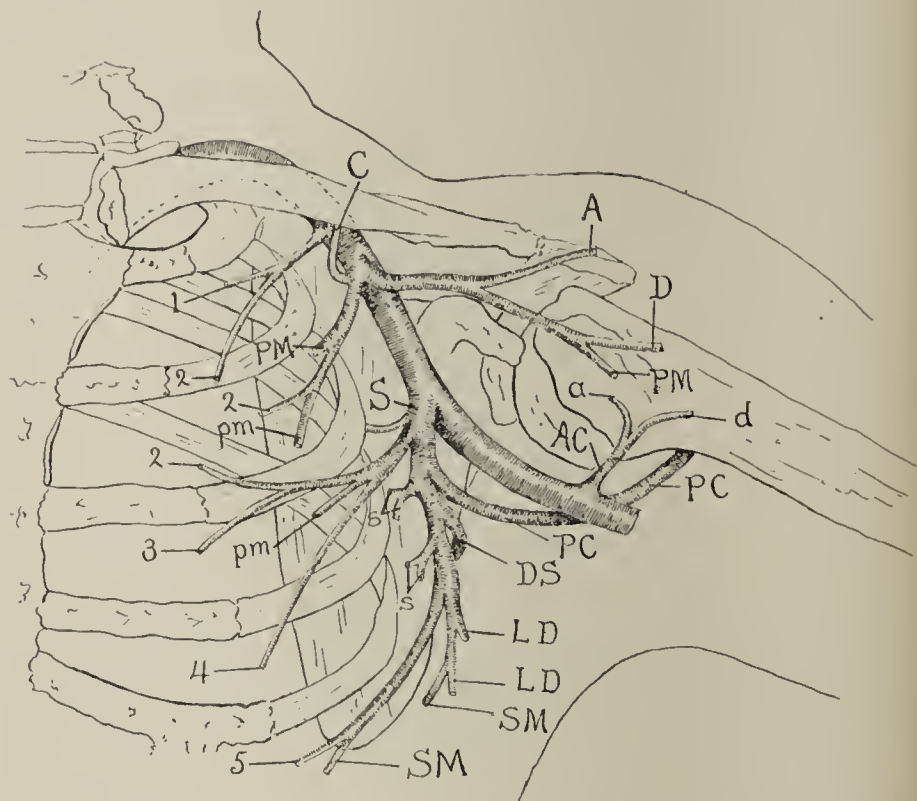


FIG. 3.—Type III of the axillary artery. Present 7 times in 47 cases.

supplies that muscle and the second, third and fourth interspaces. Just above the lower border of the pectoralis minor a larger branch descends which gives off the posterior circumflex dorsal scapular, and muscular branches and terminates in an anterior branch to the fifth interspace and serratus and a posterior branch to latissimus dorsi and serratus. From the drawing and description the thoracic branch of this artery can be seen to correspond with the description of the "long thoracic" artery, while the lower descending branch corresponds to the description usually allotted to the subscapular artery. The artery, however, can be better described as the subscapular artery because, as is seen in type I, the subscapular artery does supply the mid-thoracic region and because the long thoracic artery is so often absent. The anterior circumflex has the same origin and distribution as that given it under type I.

Part II.	No branches.	{ Dorsal scapular. Muscular.
Part III.	Subscapular	{ Anterior branch. Posterior "
	Trunk.	{ Anterior circumflex. Posterior "

The superior thoracic is small, giving a twig to the upper digitations of the serratus and ends in the first interspace.

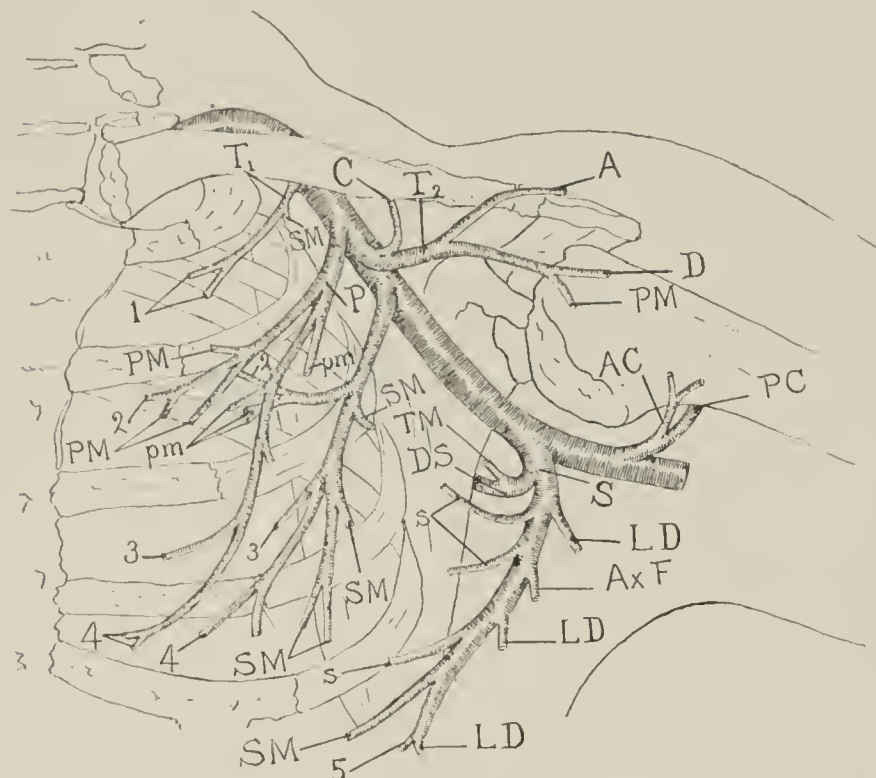


FIG. 6.—Type VI of the axillary artery. Present 2 times in 47 cases.

This type shows to a marked degree a variation which occurs in the origin of the acromio-thoracic artery, *i. e.* a separate origin of its pectoral or thoracic branch, while the artery designated as the acromio-thoracic is merely the acromio-humeral division of that artery. From the table it will be noticed (line 2, table VI) that the thoracic branch of the acromio-thoracic artery was present in one case. My notes on this case mention the fact that this branch was extremely small and that the area usually completely supplied by it receives most of its blood-supply from a branch rising from the main trunk. This pectoral branch rises from the trunk slightly above or just adjacent to the origin of the acromio-thoracic artery, courses downward and forward, supplying the pectoralis major and minor and the second, third and fourth intercostal spaces. The long thoracic artery, except for its origin, is similar to that described under type II.

The subscapular artery is the same as that of type I, and the trunk common to anterior and posterior circumflex arteries is the same as that of type II.

TYPE VII (FIG. 7 AND TABLE VII).

Type VII occurred but twice in the records made. In this type, as in type VI, the thoracic branch of the acromio-humeral artery is very small, being represented by a small twig to the pectoralis minor, while its area of distribution is supplied by a branch from the large subscapular artery; in type VI it was supplied by a separate branch from the axillary trunk.

Part I.	{ Acromio-thoracic. { Thoracic. Clavicular. Acromio-humeral. { Acromial. Muscular.
	{ Subscapular. { Pectoral. { Upper division. Lower "
	{ Muscular. Dorsal scapular. Anterior division. Posterior "
Part II.	No branches.

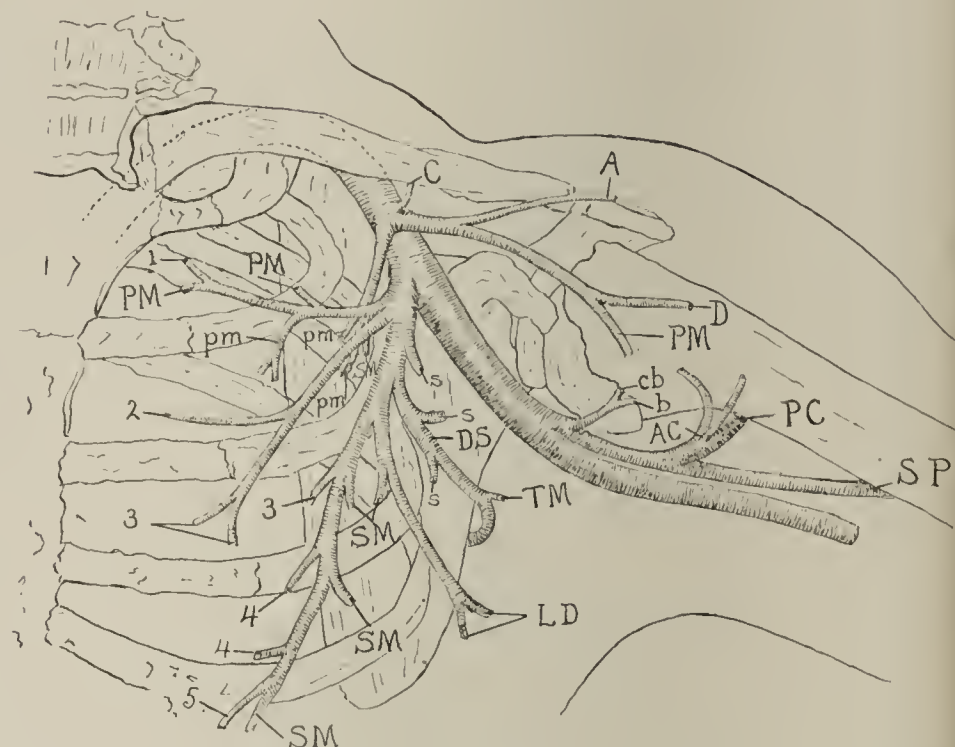


FIG. 7.—Type VII of the axillary artery. Present 2 times in 47 cases.

Part III.	Trunk.	{ Muscular branch. Trunk. { Anterior circumflex. Posterior "
		{ Superior profunda.

In this type the superior thoracic is absent and its area of distribution is supplied by the subscapular.

The acromio-thoracic is the same as type I; while the thoracic or pectoral branch is small. The subscapular arises well above the upper border of the pectoralis minor, turns downward beneath that muscle and supplies the whole thoracic, pectoral and subscapular regions. Part III gives off a large trunk which runs parallel to the main artery, gives off branches to the coraco-brachialis and biceps, and a trunk which immediately splits to form the anterior and posterior circumflex arteries (distribution similar to that under type I), and then turning down, out and back passes through the musculo-spiral groove to become the superior profunda artery.

In the first part of this paper the types into which the axillary artery fell are discussed and it is my intention in this portion to discuss the individual branches with their origin, distribution and variations.

Superior Thoracic.—This artery was remarkably constant, appearing 40 times in the 47 cases here tabulated. In the 7 cases in which it was absent it was supplied by the acromio-thoracic in 4 cases. This is the condition described as normal by Testut, Sappey and Cruveilhier. In 2 cases the subscapular supplied its area (type III), and in one case a large trunk from part II of the axillary (type V). The artery was most frequently distributed to the first and second interspaces,

as in type I. In 4 cases, however, the artery was distinctly longer than normal and rising high up in the axilla, turned directly downward and passed along the lateral thoracic wall, supplying the interspaces from 1 to 4 (in 2 cases the 5th also) and the serratus magnus muscle. This artery was in close relation to the posterior thoracic nerve, being anterior to it and separated from it by an accompanying vein. As far as can be ascertained, this artery has not been described before. In one of these cases the artery was of considerable size and gave branches to the glandular contents of the axilla and sent numerous branches forward in the intercostal spaces. In some respects it corresponds to the long thoracic, but owing to its presence in a case in which the long thoracic was present also, and its origin near that ascribed to the superior thoracic, it has been included in the description of the superior thoracic artery.

Acromio-thoracic Artery.—This branch, the most constant of the axillary subdivisions, came from part I in 40 cases, from part II in 5 cases and in the remaining 2 cases came from the trunk common to it, the subscapular and long thoracic arteries (type V). For convenience of description the following schema of the acromio-thoracic artery will be found very useful.

Acromio-thoracic.	{	Pectoral branch. Clavicular branch. Acromio-humeral branch.
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The pectoral branch of this artery was present 43 times in the 47 dissections. In the 4 cases in which it was absent its area of distribution was supplied by a pectoral branch from the axillary trunk in 3 cases (type VI), and in one case from the subscapular (type VII), which shows the thoracic branch present although small. This pectoral division of the acromio-thoracic trunk is very variable in size, occasionally being large, in which case it supplies the pectoral muscles, the second to fifth interspaces, and the serratus magnus and latissimus dorsi. In those cases in which there is a long thoracic artery present, it is smaller than in the first instance and is limited to the pectoral muscles and the upper interspaces. Occasionally it is very small, being merely a muscular branch to the pectoral muscles, and its area in this case is more completely supplied by branches from the long thoracic, the subscapular or by pectoral branches from the main trunk.

The clavicular branch is a small artery which was present 43 times in the 47 dissections. In the 4 cases in which it is absent 3 cases show no artery to this area from any of the axillary subdivisions; in one case it was supplied by a branch from the main trunk. The acromio-humeral branch is the most constant subdivision of the acromio-thoracic, and in those cases in which the pectoral branch is absent, it, with the clavicular branch, forms the acromio-thoracic artery. In the discussion of this subject under type VI, I have suggested that this artery is merely the acromio-humeral artery and not the acromio-thoracic, since it lacks the thoracic or pectoral portion. Its distribution is also constant. In one case the humeral or descending branch was small, the anterior cir-

cumflex artery in this case being large and sending off large ascending branches to the deltoid and clavicular portion of the pectoralis major. In 3 cases a branch is given off to the subscapular muscle.

The Long Thoracic.—This artery was present only 11 times as a separate branch from the axillary trunk (types II and VI) and it was with this artery that the most trouble arose in tabulating the dissections. The 11 cases here tabulated represent a large majority of the number found in all the charts received. In discussing the question of the absence or presence of a major branch from part II, it is found that in 24 cases no major branch is found, while in 23 cases there is a major trunk.

Instances in which there are no arteries from part II, type I, 20; type VI, 2; type VII, 2.

Instances in which there are arteries from part II, type II, 9; type III, 7; type IV, 4; type V, 3.

The cases in which the artery, arising from part II of the axillary is the long thoracic, are, however, less frequent, that artery being present only in the 9 cases represented by type II.

The long thoracic artery, as described by His, arises beneath the pectoralis minor, courses downward upon the serratus magnus to the fifth or sixth interspace, supplying that muscle. The external mammary branches pierce the pectoralis major and supply the skin in the mammary region. According to Testut, it arises beneath the pectoralis minor, courses obliquely downward, inward and forward along the lateral thoracic wall between the pectoralis major and the serratus magnus as far as the fifth, sixth or seventh interspace, where it terminates in anastomosis with the intercostal arteries. As it descends it gives off numerous collateral branches to the axillary glands, the subscapular muscles, the serratus magnus, pectoralis major and minor, the intercostal spaces, the mammary gland, and the antero-lateral region of the thorax. According to Quain, the long thoracic artery arises beneath the pectoralis minor, is directed downwards and inwards along the lower border of that muscle and is distributed to the pectoral muscle, the serratus magnus, and the breast, forming anastomosis with the intercostal arteries.

From the above descriptions it is readily seen how variable the distribution of the artery may be. My cases correspond more nearly to the description given by Quain, although in 3 of the cases the artery corresponded with the description given it by Testut.

The Subscapular Artery.—This artery varied considerably in its place of origin, coming from part I in 2 cases, from part II in 8 cases, from part III in 35 cases, and in 2 cases from the trunk common to it, the long thoracic and acromio-thoracic from part II. The common distribution of this artery is that given it under type I. It may, however, vary considerably, as is seen from the description given it in type III. In four cases the artery was small, being practically only the dorsal scapular artery. In these cases its remaining areas were supplied by the long thoracic in 3 cases, and by a large thoracic branch from the acromio-thoracic in one case.

(See table type I). The anterior and posterior circumflex areas are also supplied by this artery, the former in 2 cases and the latter in 9 cases. In one case it also gave rise to the superior profunda artery. The cases in which the subscapular included arteries usually arising from the axillary or brachial trunks can be classified as follows:

- Subscapular + posterior circumflex and superior profunda,
- Subscapular + posterior circumflex,
- Subscapular + anterior circumflex,
- Subscapular + anterior and posterior circumflex.

The Anterior Circumflex.—The origin of this artery was relatively constant, coming from part III as a separate branch in 22 cases and from a trunk common to it and the posterior circumflex in 21 cases. In the remaining 4 cases it took its origin from the subscapular in 2 cases, from a trunk common to it, the posterior circumflex and superior profunda in 1 case, and from the large trunk common to all the arteries in 1 case. Its distribution, as that given it under type I, was constant except in that case in which it was given off from the subscapular and supplied the area usually supplied by the humeral branch of the acromio-thoracic artery, that branch being small in this particular case. The cases in which the anterior circumflex is united with arteries ordinarily arising from the main artery may be grouped as follows:

1. Anterior and posterior circumflex,	21 cases.
2. Subscapular and anterior circumflex,	1 case.
3. " " " and posterior circumflex,	1 "
4. Trunk. { Anterior circumflex. Posterior circumflex. Superior profunda }	1 "
5. Trunk. { Acromio-thoracic. Long thoracic. Subscapular. Anterior circumflex. Posterior "	1 "

The Posterior Circumflex.—This artery was perhaps the most variable in origin of the axillary subdivisions being, however, constant in its distribution (see type I).

- The places of origin are as follows:
1. From axillary artery, 13 cases.
2. Trunk. { Anterior circumflex.
Posterior " }
3. Subscapular. 9 "

4. Trunk.	{ Posterior circumflex. Superior profunda. }	2 "
5. Trunk.	{ Acromio-thoracic. Long thoracic. Subscapular. Anterior circumflex. Posterior "	1 "
6. Brachial artery.		1 "

The 3 trunks recorded in the table have been described elsewhere in this paper and are sufficiently clear from the table itself. The remaining muscular, cutaneous and intercostal branches are infrequent and may or may not occur. When present they are large or small as the case necessitates. The branch labelled "axillary fascia" is that which is usually described as the alar thoracic artery. It was present 8 times, its area being supplied by the larger subdivisions of the main arteries in their courses through the axilla.

The Posterior Scapular.—This artery arose from the axillary artery in 5 cases. The artery in its course turns backward, passes either between the trunks of the brachial plexus or passes over them, courses along the superior margin of the scapula and then turns downward to pass parallel to the vertebral margin of the scapula. In its course it gives branches to the subscapularis, levator anguli scapulæ, trapezius, rhomboid major and rhomboid minor, supraspinatus and infraspinatus.

The suprascapular artery was found arising from the axillary artery in one case. In one case the superior profunda was given off in the axilla. In two cases not included in these records the axillary artery divided into the radial and ulnar in the axilla, and in these cases the anterior and posterior circumflex arteries and the superior profunda were given off by the radial.

- The conclusions to be drawn from this study are:
- (1) That while the origin of the subdivisions of the axillary artery varies, the distribution is practically constant.
- (2) That type I, as here described, is the ordinary form in which the axillary artery is found.
- (3) That the long thoracic artery and alar thoracic arteries are most frequently absent and that their areas of distribution are supplied by the adjacent branches from the main artery.

TABLE SHOWING THE ORIGIN AND DISTRIBUTION OF THE BRANCHES OF THE AXILLARY ARTERY IN FORTY-SEVEN CASES.

BRANCH.	ORIGIN.			DISTRIBUTION.																									
	Part I.	Part II.	Part III.	1st Intercostal space.	2nd Intercostal space.	3rd Intercostal space.	4th Intercostal space.	5th Intercostal space.	Pectoralis major.	Pectoralis minor.	Pectoralis major, acromion, and deltoid.	Subclavius and clavicle.	Subscapularis.	Dorsal region of scapula.	Serratus magnus.	Latissimus dorsi.	Teres major.	Posterior circumflex.	Anterior circumflex.	Axillary glands and fascia	Coraco-brachialis.	Biceps.	Articular.	Posterior region of scapula.	Superior profunda.	Teres minor.	Deltoid.	Suprascapular.	
Superior thoracic.....	40	40	26	9	4	2	1	..	5	
Acromio-thoracic.....	40	5	..	7	24	24	6	2	41	38	45	43	3	..	2	1	
Long thoracic.....	2	9	..	1	4	11	11	5	1	8	5	..	11	3	
Subscapular.....	2	8	35	2	6	22	32	41	1	8	42	45	41	41	23	9	2	2	1	1	

BRANCH.	ORIGIN.			DISTRIBUTION.																								
	Part I.	Part II.	Part III.	1st Intercostal space.	2nd Intercostal space.	3rd Intercostal space.	4th Intercostal space.	5th Intercostal space.	Pectoralis major.	Pectoralis minor.	Pectoralis major, acromion, and deltoid.	Subclavius and clavicle.	Subscapularis.	Dorsal region of scapula.	Serratus magnus.	Latissimus dorsi.	Teres major.	Posterior circumflex.	Anterior circumflex.	Axillary glands and fascia	Coraco-brachialis.	Biceps.	Articular.	Posterior region of scapula.	Superior profunda.	Teres minor.	Deltoid.	Suprascapular.
Anterior circumflex	22	22
Posterior circumflex	13	13
Trunk common to anterior and pos- terior circumflex	21	21	21
Trunk common to circumflex arteries and superior profunda	2	2	1	..	1	1	2
Common trunk	15	5	1	..	2	2	2	2	2	2	2	2	21	2	2	2	2	1	1	1	..	1	1	2
To subscapularis	1	1	1
To serratus magnus	2	2	4
To pectoralis major	3	6	9
To pectoralis minor	5	1	4	3	2	..	5	5	1	1	1
Pectoral branch	1	2	1	9
To subclavius and clavicle	1	2	5	2
To axillary fascia	2	3	4	8
Articular	1	1
1st and 2nd interspaces	1	1
2nd interspace	1	1
2nd and 3rd interspaces	1	1	..	1	2	2
To coraco-brachialis	1	19	20
To biceps	1	19	20	20
To deltoid	1	1	5	..	2	..	1
Posterior scapular	5
Suprascapular	1
Superior profunda	2	2

TYPE I, 20 CASES.

BRANCH.	ORIGIN.			DISTRIBUTION.																				REMARKS.			
	Part I.	Part II.	Part III.	1st Interspace.	2nd Interspace.	3rd Interspace.	4th Interspace.	5th Interspace.	Pectoralis major.	Pectoralis minor.	Pectoralis major, acromion deltoid.	M. subclavius.	M. subscapularis.	Dorsal region of scapula	M. serratus magnus.	M. latissimus dorsi.	M. teres major.	Posterior circumflex.	Anterior circumflex.	Axillary glands and fascia.	M. coraco-brachialis.	M. biceps.	Articular.		Posterior region of scapula	Superior profunda.	Teres minor.
1. Superior thoracic	19	19	14	5	1	1	..	2	In the absent case the region was supplied by the acromio-thoracic artery.
2. Acromio-thoracic	20	2	12	15	5	2	20	20	20	19	2	..	2	1	
3. Subscapular	20	12	19	19	..	1	17	20	19	19	12	4	..	1	1	1	
4. Anterior circumflex	12	12	8. times from a branch common to circumflex arteries (see line 6). 8 times from branch common to circumflex arteries, 4 times from subscapular, 1 case from brachial artery (see lines 3 and 6).
5. Posterior circumflex	7	7	
6. Trunk common to anterior and posterior circumflex arteries..	8	8	8	
7. To M. subscapularis	2	2	11	
8. To pectoralis major.....	2	2	4	
9. To pectoralis minor.....	2	2	5	
10. Axillary glands and fascia.....	1	2	2	5	
11. Articular.....	2	1	2	5	
12. 2nd and 3rd interspaces	1	1	..	2	2	
13. Coraco-brachialis	10	10	
14. Biceps	10	10	
15. Posterior scapular	2	2	

TYPE II, 9 CASES.

BRANCH.	ORIGIN.			DISTRIBUTION.																				REMARKS.			
	Part I.	Part II.	Part III.	1st Interspace.	2nd Interspace.	3rd Interspace.	4th Interspace.	5th Interspace.	Pectoralis major.	Pectoralis minor.	Pectoralis major, acromion, deltoid.	Subclavius.	M. subscapularis.	Regio dorsalis scapulae.	M. serratus magnus.	M. latissimus dorsi.	M. teres major.	Posterior circumflex.	Anterior circumflex.	Axillary glands and fascia	Coraco-brachialis.	Biceps.	Articular.		Posterior region of scapula.	Superior profunda.	Suprascapular.
1. Superior thoracic	2			7	4	2	1																				{ Absent twice, supplied by acromio and long thoracic (see lines 2 and 3). Pectoral branch absent twice, area supplied by long thoracic (line 3) and pectoral branch (line 11).
Acromio-thoracic	9			2	3	2			7	6	9	2															
3. Long thoracic.....	9			1	2	9	9	5	1	6			5		9	3				3							
4. Subscapular		9				3	6						9	9	6	6	6	1	1	1							{ Large in 3 cases, supplying the subscapular area in part (see line 4). Small in 3 cases, being confined to dorsal and scapular region principally (see text). For remaining place of origin see lines 4 and 7. For remaining places of origin see lines 4, 7 and 8.
5. Anterior circumflex.....			4																4								
6. Posterior cireumflex.....			3															3									
7. Trunk, common to anterior and posterior circumflex arteries			4															4	4								{ For other origins of circumflex arteries, see lines 4, 5, 6 and 8.
8. Trunk			1															1							1		
9. Branch to M. subscapularis.....	3	1	1										5														
10. To serratus magnus.....	1														1												
11. Pectoral branch.....	2	1		1	1				3	2																	
12. Articular.....		1																					1				
13. Coraco-brachialis			3																		3						
14. Biceps			3																			3					
15. Suprascapular	1																								1		

TYPE III, 7 CASES.

1. Superior thoracic.....	6	6	5	2	2	2																					{ Absent once, supplied by acromio-thoracic and sub- scapular.
2. Acromio-thoracic.	7		2	4	3		7	6	7	7																	
3. Subscapular	7		1	4	5	7	7		5		7	7	7	7	3	2											
4. Anterior circumflex			4													4											{ For 3 remaining cases see line 6. From subscapular in 3 cases. From trunk (line 6) in 3 cases.
5. Posterior circumflex.....			1												1												
6. Trunk, common to anterior and posterior circumflex.....			3												3	3											
7. M. subscapularis.....	2										2																Sec lines 4 and 5.
8. M. coraco-brachialis.....		1	2														3										
9. M. biceps.....		1	2																3								
10. Articular.....		1	1																		2						
11. 1st and 2nd interspaces.....	2			2	2																						
12. Br. to deltoid.....		1	1																						2		
13. M. pectoralis minor.....		1								1																	
14. Axillary fascia.....			1													1											
15. Superior profunda.....			1																						1		
16. Posterior scapular	1																							1			

ORIGIN.	DISTRIBUTION.
Part I.	
Part II.	
Part III.	
1st Interspace.	
2nd Interspace.	
3rd Interspace.	
4th Interspace.	
5th Interspace.	
Pectoralis major.	
Pectoralis minor.	
Pectoralis major, acromion, deltoid,	
M. subclavius.	
M. subscapularis.	
Regio-dorsalis scapular.	
M. serratus magnus.	
M. latissimus dorsi.	
M. teres major.	
Posterior circumflex.	
Anterior circumflex.	
Axillary glands and fascia	
M. coraco-brachialis.	
M. biceps.	
Articular.	
Posterior region of scapula	
Superior profunda.	

[illegible][illegible][illegible][illegible]

ON THE ORIGIN OF THE LYMPHATICS IN THE LIVER.

BY FRANKLIN P. MALL,

Professor of Anatomy, Johns Hopkins University.

The origin of the lymphatics of the liver was first definitely determined by MacGillavry,¹ who studied this subject under the direction of Ludwig. Long before the work of MacGillavry it had been observed that ligation of the bile duct was followed by passage of bile over into the lymphatics, and the artificial filling of the lymphatics naturally followed by injecting a colored fluid into the bile duct. Sections of liver, in which the lymphatics had been filled with Prussian blue, or with asphalt, showed that the fluid injected into the bile ducts leaves them at the periphery of the lobule to enter spaces surrounding the blood capillaries, the so-called perivascular lymph spaces. These spaces communicate at the periphery of the lobule directly with the interlobular lymph channels. Frequently there is an extravasation of the injection mass into the blood capillaries of the lobule.

These observations were subsequently confirmed by numerous competent investigators, using the method employed by MacGillavry as well as that of direct injection of Prussian blue into the walls of the portal and hepatic veins. In successful injections made in this way it is found that the Prussian blue injected enters the lobule to encircle its blood capillaries.² Such injections, however, are always accompanied with numerous extravasations of the injected material into the tissues between the lobules, and often there is a secondary injection into the blood capillaries of the lobule. This fact has raised an objection to the direct injection of the lymphatics from the bile capillaries. It appears more probable, the opponents say, that the extravasation of bile, or the injected material into the interlobular spaces, enters the lymphatic radicals of the capsule of Glisson, and from them the larger lymph channels and the perivascular spaces of the capillaries are filled. Furthermore the injected mass may pass from the pericapillary spaces directly into the capillaries, thus accounting for their frequent injection.

According to Fleischl,³ all the bile is taken up by the lymphatics after ligation of the bile duct, and in case the thoracic duct is also ligated no bile or only a trace of bile ever reaches the blood. The observation of Fleischl has been confirmed by Kunkel,⁴ Kufferath⁵ and Harley.⁶ It is extremely difficult to understand why the bile does not enter the blood capillaries in case it passes from the bile capillaries over into the perivascular spaces before it reaches the interlobular spaces after ligation of the bile duct. A further objection to the idea that the perivascular spaces first take up the bile, after ligation of the duct, is the fact that fluids

injected into the bile duct pass with ease over into the lymphatics but only with difficulty into the bile capillaries. In all cases it appears as if the main origin of the lymphatics is at the periphery of the lobule and that the radicals communicate freely with the perivascular lymph spaces. Furthermore, it appears that the course the bile takes after ligation of the bile duct, or of a fluid injected into the bile duct in passing to the lymphatics, is between the lobules or at least at their extreme periphery. This idea is greatly strengthened since we know that the walls of the capillaries of the lobule are extremely porous, being composed of a dense layer of reticulum fibrils⁷ upon which lie the endothelial or Kupffer's cells. This layer of reticulum fibrils encircling each capillary has been described from time to time by many investigators, and has been isolated by Oppel⁸ and by myself.⁹ Oppel obtained clear pictures of the connective tissue of the liver lobule by means of silver precipitation, while I employed Kühne's method of pancreatic digestion to remove the cells, followed by some intense stain like acid fuchsin. The nature of these fibrils is still under discussion but that matters little for the present communication. It is sufficient to know that the fibrils of reticulum form a basket-like membrane surrounding each capillary of the whole lobule, the interior of which is only partly lined by Kupffer's syncytial endothelial cells. The capillary walls then are very pervious, blood plasma passing easily from them out into the perivascular spaces to bathe the liver cells.

It is well known that a large quantity of lymph is constantly passing from the liver, much more than from any other organ. That this lymph comes directly from the blood is indicated by its high per cent of proteid matter, nearly that of the blood, and from two to three times that of the lymph from other parts of the body.

The course the lymph takes from the blood to the lymph radicals, *i. e.* its natural course, can easily be marked by injecting colored gelatin into any of the blood-vessels. I have usually found it most convenient to inject the gelatin into the portal vein, but it is just as easy to fill the lymphatics by injecting either the hepatic artery or hepatic vein. In all cases the colored fluid reaches the main lymph channels in the same way. The colored gelatin flows with great ease from the capillaries at the periphery of the lobule as well as from those around the sublobular vein into the lymphatics. After the lymphatics have all been filled it is well to inject a small quantity of fluid of different color into the blood-vessels. A much better method of making double injections is to mix red granules with a blue gelatin or blue granules

¹ MacGillavry, Wiener Sitzungsber., 1864.² Budge, Ludwig's Arbeiten, 1875.³ Fleischl, Ludwig's Arbeiten, 1874.⁴ Kunkel, Ludwig's Arbeiten, 1875.⁵ Kufferath, Arch. für Physiol., 1880.⁶ Harley, Archiv für Physiol., 1893.⁷ Kupffer, Arch. f. Mik. Anat., 54.⁸ Oppel, Arch. Anz., 1890.⁹ Mall, Abhandl. d. K. S. Ges. d. Wiss., xvii, 1891.

with a red gelatin, the fenestrated lining membrane of the capillary acting is a sieve which allows the fluid to pass but holds back the granules, as is the case with the blood when normal circulation is taking place.

If the portal vein is injected with Prussian-blue gelatin under a low pressure, it is found that in a few minutes the lymphatics are all filled with the blue mass. Livers injected in this way are best hardened in formalin and then cut by the freezing method, for alcohol causes the gelatin to shrink. Such sections show that the blue fluid has entered the lymphatics at the periphery of the lobule. More instructive are the specimens when the injection is stopped just as the first lymphatics are filled with the colored gelatin. By following the larger lymphatics back into the liver substance it is found that the interlobular connective tissue is entirely filled with blue where the lymphatics are injected, but only partly colored blue when they are not. In other words, the blue extra-

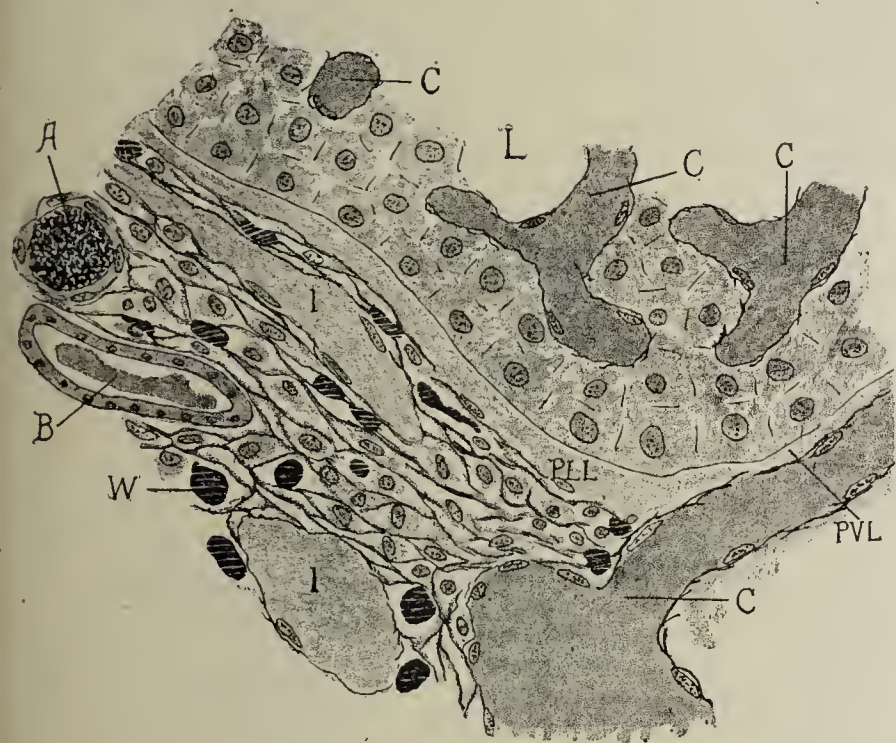


FIG. 1.—Section through the periphery of the liver lobule of a cat. The hepatic artery was injected with cinnabar gelatin, and the portal vein with Prussian-blue gelatin, stained with Van Gieson's stain. $\times 500$ L, lobule of liver; c, capillaries; a, artery; l, lymph vessel; pvl, times. perivascular lymph space; pll, perilobular lymph space; w, bundles of fibrils of white fibrous tissue.

vasates from the periphery of the lobule, invades the connective tissue until it reaches the beginning of the lymphatics, when of course it is carried rapidly from the liver. The nearest course from the lobules to the lymphatics is between the lobule where the amount of connective tissue is small, so when colored fluid is beginning to enter lymph channels the tips of the capsule of Glisson are entirely colored, while larger portal spaces are encircled by a zone of the color. Furthermore it is found that in certain instances when the injection was not continued long enough the blue did not enter the lymphatics. In such specimens it is found that all the interlobular spaces are surrounded by a zone of colored gelatin which does not enter the main lymph channels.

A successful injection of the lymphatics is illustrated in the accompanying figure. The section was stained with Van Gieson's stain which gives a very satisfactory result. The granular blue enters the capillaries of the lobule, c, with ease,

and from them the liquid blue is filtered through the capillary walls to enter the perivascular lymph space. This space communicates at the periphery of the lobule directly with a large lymph space between the liver cells and the capsule of Glisson, which I shall term the perilobular lymph space. These spaces in turn communicate with the lymph radicals.

Injection of the blood-vessels of the liver with aqueous Prussian blue fills the capillaries only, and in all cases it is shown that there are no capillaries between the periphery of the lobule and the interlobular connective tissue. The liver cells come directly against the capsule of Glisson. An injection of brief duration with blue gelatin soon fills the perilobular lymph spaces, so that it appears as if all groups of liver cells at the periphery of the lobule were separated from the interlobular connective tissue with capillaries. In case cinnabar granules are mixed with the blue a few of these granules are found in the perivascular and perilobular lymph spaces. The openings in the walls of the capillaries are large enough to allow a few of the smaller granules to pass through. As the injection is continued the blue invades the connective tissue spaces from the lymphatic radicals more and more until a lymph channel is reached, when of course it flows rapidly from the liver. Were there a direct channel from the perilobular lymph spaces the blue should flow through it at once without further filtration through the interlobular connective tissue spaces. The course the cinnabar granules take also speaks against a direct channel between the perilobular lymph spaces and the interlobular lymph channels. A few of the granules enter the perilobular lymph spaces, but none of them reach the main lymph channels. All of my specimens without exception force me to the conclusion that there are no direct channels connecting the perivascular and perilobular lymph spaces with the lymphatics proper other than the ordinary spaces between the connective-tissue fibrils of the capsule of Glisson. These spaces, however, are relatively large, permitting of a rapid diffusion through them.

Interstitial injections into the walls of the interlobular veins naturally fill the surrounding lymphatic vessels, and when no valves are in the way the injected fluid passes to the origin of the vessels, or lacunæ, which are only in part lined with endothelial cells. From here the fluid passes through the main connective-tissue spaces to the periphery of the lobule into the perilobular and perivascular lymph spaces, and frequently from them into the blood capillaries. When the injection is made through the bile ducts I have always found that there is an extravasation of the fluid from these at the periphery of the lobule which immediately enters the lymph radicals, although the bile capillaries are often injected well into the lobule. The extravasation does not take place from the bile capillaries, only from the duct as it communicates with the capillaries; also it does not take place from the larger bile ducts. Such extravasations naturally are picked up by the lymphatics and are at once carried from the liver. If after ligation of the bile duct the bile enters the perivascular lymph space within the lobule it may still be carried to the

lymphatics, as the direction of the current of lymph is constantly from the blood capillaries to the lymphatics.

It is well known that the liver cells arise from the embryonic bile ducts, and that in the further growth of the liver the bile ducts must elongate in order to adjust themselves with the growing liver. Hendrickson¹⁰ has shown by staining the bile capillaries and ducts of the embryo's liver by Golgi's method that the tip of the primitive bile duct is added to by a coalescence of the bile capillaries at the periphery of the embryonic liver lobule. My own observation on the liver lobule after it is well formed is that whenever karyokinetic cell figures are present they are at the periphery of the liver lobule, *i. e.* at the junction of the bile capillary with the bile duct. It also appears that the vascular walls of the embryo are much more pervious than those of the adult, judging by the ease extravasation takes place when the blood-vessels of embryos are injected. This observation taken with that of the growth of the bile ducts may be an explanation why the extravasation of a fluid injected into the bile duct takes place at the periphery of the lobule. A further hint in this direction is the observation that it is easy to inject the lymphatics from the blood-vessels of an inflamed area. I have often seen the lymphatics of an inflamed intestine filled with blood, and upon injecting the blood-vessels found that the fluid readily entered the lymphatics.¹¹

¹⁰ Hendrickson, Johns Hopkins Hospital Bulletin, 1898.

¹¹ See also Sigmund Mayer, *Anat. Anz.*, 1899.

That the capillaries of the liver communicate more freely with the lymphatics than do the bile ducts is proved by injecting the bile duct and the portal vein with fluids of different color under the same pressure at the same time. In all the experiments I made the fluid injected into the vein appeared in the lymphatics first. In many instances beautiful injections of the lymphatics were obtained from the vein while the fluid injected into the bile duct did not extravasate at all, showing at least that the veins communicate with the lymphatics much more freely than do the bile ducts.

The conclusions to be drawn from the above observations are (1) that the lymphatics of the liver arise from the perilobular lymph spaces and that these communicate directly with the perivascular lymph spaces; and (2) that the lymph reaches these spaces by a process of filtration through openings which are normally present in the capillary walls of the liver. Furthermore, the fluid injected into the lymphatics from the bile duct leaves the duct as it enters the lobule and is at once taken up by the lymph radicals and perilobular lymph spaces, and from them extends, as a secondary injection, to the perivascular lymph spaces, and often into the blood capillaries of the lobule. The larger lymphatics accompanying the portal vein arise between the lobules near their bases, while those accompanying the hepatic vein do not arise within the lobule but around the larger sublobular veins.

BORN'S METHOD OF RECONSTRUCTION BY MEANS OF WAX PLATES AS USED IN THE ANATOMICAL LABORATORY OF THE JOHNS HOPKINS UNIVERSITY.

BY CHARLES RUSSELL BARDEEN,

Associate in Anatomy, Johns Hopkins University.

The wax-plate method of reconstruction (*Plattenmodellen methode*) described by Born in 1876¹ has proved of great value in the study of the morphology of embryos. The method has received its most extensive application in the hands of Born, of His and of various pupils of these investigators. In general, however, it may be said, that the value of this method as an aid to the microscopic study of form has not been sufficiently appreciated.

In part this lack of a more general application of the method has been due to certain technical difficulties which tend to make it cumbersome and time-consuming. Yet by no other method can so accurate an idea be obtained of the form of those structures which from their minuteness or complexity of relation cannot well be dissected out.

Considerable application of the method has recently been made by different persons in this institution and each worker has contributed something towards making the method more effective.

As originally described by Born several steps are essential for the successful application of his method. These may be tabulated as follows:

A. Preliminary steps.

1. Obtaining a good picture of the embryo or object to be reconstructed.
2. Hardening, staining and sectioning the object.
3. Drawing magnified enlargements of the sections or such parts of them as it is desired to reconstruct.
4. Preparation of the wax plates.
5. Transference of the image to the surface of the wax and cutting out the wax plates.

B. Constructing the model.

1. Piling the wax plates.
2. Removing parts not essential to the reconstruction desired and rounding off of the parts reconstructed.
3. Strengthening and finishing the model.

I shall consider these steps in the order named.

A. Preliminary steps.

1. Before proceeding to section the object to be recon-

¹ *Morph. Jahrb.* 11; *Arch. f. mikr. Anat.*, xxii, p. 584.

structed it is important to obtain good pictures of its external form. With such a picture at hand it is much easier to pile up the wax plates which represent the sections through the object. This is especially true when the object is symmetrical, as in the reconstruction of embryos, profile views of which are invaluable in this work. If the picture be enlarged to the magnification of the model desired a valuable control is furnished. A series of parallel lines may then be drawn through the picture to represent the planes through which the knife has passed in sectioning the embryo, so that the position of every plate is indicated.

For general purposes photography is undoubtedly the most convenient method of recording the gross external features of the object. If the object be very small as, for instance, an early human embryo, the camera may be so placed that the image in the negative is enlarged from two to four diameters. It is found that the most convenient way of photographing embryos is to place the camera with the axis in a vertical direction and the lens pointing downwards. A stand for holding the camera in this position and raising or lowering it is easily constructed. Ordinary lead shot seems to be especially good for holding many small objects in the position in which it is desired to photograph them.

For detail in the distant as well as the proximal part of the object it is a great aid to make use of a stand capable of being raised without moving the object laterally. In this way, if the diaphragm be closed down so as to make the exposure a long one, the object may from time to time be brought slightly nearer to the lens of the camera, so that parts more distant are brought into sharp focus.

From the photographic plates thus obtained lantern slides are made or the negative itself is used to project the image at the required magnification upon a screen. Free-hand drawings are then traced on a paper upon which the image falls, or, if desired, bromide enlargements can be made. In this way accurate records can quickly be made of the external appearance of the object to be studied, yet no special talent for drawing is required. In the study of embryos the profile view is the most essential one, though others also prove of great value.

2. The only real essentials in the technique of obtaining serial sections of the object to be studied are that the series should be complete, the sections perfect and of uniform thickness. As pointed out by Born, the most convenient sections for this work are those from 20-40 microns in thickness. For sections of this thickness we have found alum cochineal to give uniformly the most satisfactory stain. It is important to know which side of the sections was uppermost during the cutting, so that in the subsequent reconstruction a true and not a mirror image of the object will be formed. For this reason it is well to make it a uniform practice to begin at the head when cutting transverse sections through an embryo, at the right side when cutting longitudinal vertical sections, and at the dorsal side when cutting horizontal sections and to label the sections in the order in which they have been cut.

3. For making drawings of the sections we have found that in general a projection apparatus is more convenient than a camera lucida unless the sections are small. Our projection apparatus is set up in a large dark room.

The illumination is received from an arc electric light or from a heliostat. An ordinary microscope stand with the tube in a horizontal direction is used when the sections are small and a high magnification is desired. Eye piece and draw tube are usually removed and the objective is used as the magnifying lens. In case of larger sections a projection lens similar to that used for lantern slides is utilized.

The image is projected upon a screen which runs on a track. The screen can be moved toward or away from the microscope by means of windlass situated near by. In this way any desired magnification can be quickly obtained by using an appropriate lens and bringing the screen into the proper position.

The screen which I devised for our dark room has attached a leaf which can be lowered so as to form a drawing table and a mirror that can be placed at an angle of 45° over the table. In this way the image is projected on a horizontal surface so that tracing it is easier than when it is upon a vertical surface. In using an ordinary mirror a double image is projected but that from the surface of the mercury is so much brighter than that from the surface of the glass that no difficulty is experienced in drawing accurate outlines.

Fig. 1 illustrates the apparatus here in use.

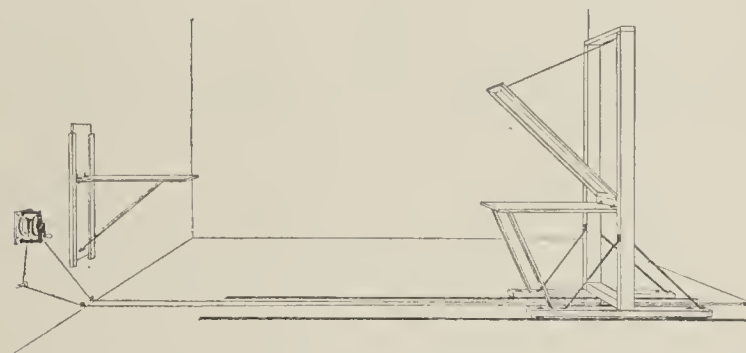


FIG. 1.—At the right the projection screen is shown in position on the track. The mirror is lowered to an angle of 45° and the drawing table is extended horizontally below this. At the left are shown the windlass used for moving the projection screen and the shelf used for holding the projection lantern.

In drawing pictures of the sections a careful outline of those main features which it is desired to bring out in the reconstruction is the great essential. In addition it is often of value to distinguish by using pencils of various colors the different organs in structures as they appear in the section.

If desired, direct bromide enlargements can be made of the sections on the slides. This is the method preferred by His. The simpler method described above we have found, however, to be more convenient for general purposes.

The outline drawings may often be elaborated to any desired extent when the sections are subjected to careful microscopic study. It is a great help for the subsequent reconstruction to label, so far as possible, the various structures in the outlines of the sections before proceeding to the wax plates.

4. Much trouble in the preparation of the wax plates is to be saved by using plates of a uniform thickness and by making the magnification of the object under reconstruction correspond. The most convenient thickness for general use is 2 mm. Occasionally, for coarser work, 4 mm. plates have proved of value. It is very easy, with the apparatus above described, to make the ratio of the diameter of magnification of the drawings to the diameter of the sections equal to that of two millimetres to the thickness of the section. If plates 2 mm. thick be used and every section be drawn, sections 20 mm. thick = $1/50$ mm. must be magnified one hundred times. Or if desired, as is more often the case, every other section may be drawn at a magnification of fifty diameters.

For making the wax plates we have a large zinc pan with vertical sides. Its surface area is such that one kilogram of the wax mixture which we use will make a plate 1 mm. thick. The method of casting the plates is essentially that described by Born. Boiling water is run into the pan to the depth of several inches. On the surface of this the hot melted wax mixture is poured and quickly forms an even, smooth layer. Bubbles, which occasionally appear in the wax, may be quickly exploded by turning the flame of a Bunsen burner on the surface of the wax where they appear. As the wax plate cools it is necessary to free it from the sides of the pan by running a knife along the edge. Before the plates are perfectly cool they may readily be cut into smaller plates of any desired size.

The wax mixture in use here is composed of 950 parts of bees-wax and 50 parts of white rosin. Often, especially in summer, paraffin is added to give additional toughness. Black plates are made by adding lamp black to the melted wax, until after thorough stirring the mixture has become uniformly black. The amount by weight of wax necessary for a plate of a given size is obtained more easily by experimental trial than by calculation. A certain amount of wax becomes attached to the sides of the pan by surface tension, so that slightly more wax must be used than the amount one is likely to determine by calculation from the specific gravity of the wax and the size of the pan. On the other hand if a pan of a given size be used the amount of a given wax mixture necessary for making a plate of given thickness may be determined by a few trial castings.

The outlines are transferred to wax by means of red or blue tracing paper. The wax plates are then placed upon glass and are cut with a small, narrow knife and in a warm room.

B. Constructing the model.

1. The janitor can be trusted to trace the outline drawings on wax, to cut through the wax with a sharp knife where the outlines are traced and to make the preliminary piling. Usually two preliminary piles are made, one of that part of the wax plates which represent the sections and one of the wax plates themselves after removal of the parts representing the sections. From the former a positive, from the latter a hollow negative image of the original object is ob-

tained. In this piling an enlarged picture of the object is of very great help. As originally suggested by Born, in case of symmetrical objects a surface outline may be drawn on card board and cut out, thus giving a fixed ridge against which to pile the plates. If but one side of any embryo is to be reconstructed from transverse sections it is of great help to cut each plate off sharply at the midline and to pile the plates against a profile outline of the embryo situated on a board which has been placed perpendicular to the plane in which the plates are piled. In case the reconstruction of some internal organ is wanted it is usually of advantage to reconstruct at the same time the external form of the object, so that when the plates are piled the image they form may be compared with the picture of the original object. After getting the plates composing the positive image of the object into proper position, it is easy to trace two or three of its surface curves on paper or to represent them in wire and then to get the negative formed, as described above, into true shape. Plaster casts can then be made in this negative mould. The plaster casts, representing the external features of the original object, are very valuable to have at hand, while engaged in reconstructing the internal features from the wax plates.²

The method of making every fifth plate a black one has proved to be extremely valuable in arranging the wax plates. In this way it is easy at any time during the reconstruction of the model to count up and place any given section.

The method of reconstruction which I have found most convenient is as follows: After the plates are placed in proper position so that the external features of the object are accurately portrayed, I begin by taking off five plates from one side. The drawings of the sections I likewise have pinned together in groups of five in the same order in which the plates are piled. By going over the five finished drawings it is easy to obtain a good conception of the form of the structures represented in the block of five plates under consideration. I have at hand a paper of fine pins and these I press down through the various structures seen in section on the surface plate, and in such a direction that they will pass into the same structure in the sections below. When the parts of the plates which represent the structures to be reconstructed are thus firmly united by pins I remove the intervening portions of the wax plate with a pair of forceps. Thus, in a very short time, one is enabled to bring to light the form of the structures lying within the block of five sections. The pins hold the various bits of wax firmly in place and serve to strengthen the model in every way. When I feel satisfied with the appearance of the structures in the first block of five sections I proceed to the next and treat it in the same way. Those structures which are cut in both blocks of sections may at the same time be pinned together. After two or three blocks of sections have thus been piled up it is often well before adding another block of five sec-

² Many methods have been devised of piling plates according to special marks. The method devised by Wilson, *Zeitschrift für wissenschaftliche Mikroskopie*, xvii, 1900, page 177, seems a good one.

tions to fuse them together with a hot knife and thoroughly to strengthen the reconstruction so far as it is completed. For strengthening piles of narrow strips of wax, representing sections through membranes and the like, a wire netting is of the greatest value. Perhaps the best form of wire netting for general purposes is a copper netting with 10 strands to the centimetre. The copper netting has no tendency to cause subsequent warping, as is the case with iron netting. The netting is heated in the flame of a Bunsen burner and is then applied to the surface which it is desired to strengthen. In case of narrow columns, such, for instance, as are formed in the reconstruction of blood-vessels and nerves, copper wire is of the greatest value. This can be heated and sunk in at one side and then fused over.

After the model is once well started the subsequent building up can proceed with great rapidity. Plates in blocks of five are added as described above until the model is finished. Of course a greater or less number of plates than five may be used to a block. In most of my work, however, I have found blocks of five, with a black plate on the surface of each block, to give the most satisfactory results.

In order to keep the various structures distinct during the reconstruction it is often of value to paint them with different colors, while the work proceeds. The various structures of a model built up as described may be removed as completed, or during the course of reconstruction, and then readily replaced. Pins are of great value in holding structures in

place and for indicating where a structure removed must be replaced in order to regain its proper position.

If it is desired at any time to cut the model in a given direction the pins which hold the pieces of wax together may be readily cut with scissors.

3. I have mentioned methods by which the model is greatly strengthened during the course of reconstruction, the use of pins, of wire netting and of wire. All three means may be employed thoroughly to strengthen the model after the first rough reconstruction. The wire screening is then especially valuable. Of course it is possible to add free hand and with a good deal of accuracy structures which from their delicacy are difficult to model. This is true of blood-vessels, nerves and of fine membranes. The blood-vessels and nerves may be readily constructed by covering copper wire with wax, the membranes by covering a netting of narrow meshes with a thin coating of wax.

In rounding and smoothing up various structures in a model so as to give it a finished appearance, semi-melted wax applied with the fingers or with a spatula is of the greatest help.

The model is greatly protected in many ways by a thick coating of paint. Hot weather seems to have a far less detrimental effect on such models than on models unpainted.

We have found photography of great help not only in recording the condition of the finished model but also, at times, during the course of a reconstruction.

MODEL OF THE NUCLEUS DENTATUS OF THE CEREBELLUM AND ITS ACCESSORY NUCLEI.

BY HARRY A. FOWLER.

(From the Anatomical Laboratory of the Johns Hopkins University.)

At the suggestion of Dr. Barker I have undertaken the study of the central gray matter of the cerebellum and its relations to the white fibre bundles to which it is intimately related. It has seemed advisable to make a partial report including a reconstruction in wax of the nucleus dentatus and its accessory nuclei.

In a study of the internal structure of the cerebellum it is necessary to consider the work of Stilling on this region. To him belongs the credit of being the first to study the internal anatomy of the cerebellum by means of serial sections made in various planes and stained with dyes to bring into greater contrast the white matter and the gray masses. With the crude methods at his disposal for preparing serial sections and staining them, the drawings of Stilling show with remarkable accuracy the relations of these central nuclei to the white substance in which they lie buried and to which they are closely related.

The Material.—The model was made from a series of transverse sections through the medulla and cerebellum of a new-born babe prepared by Dr. John Hewetson in the Anatomical Laboratory of the University of Leipzig. The material was hardened in Müller's fluid, cut 70 μ thick, and stained by the

Weigert-Pal method. Every other section was used and hence each section represents a thickness of 140 microns. A series of sagittal sections through the medulla and cerebellum of a new-born babe was also prepared and treated in a similar way for use as a control in measurements and to furnish an outline of the floor of the fourth ventricle. This outline was used in building up the model.

The Method.—Born's method for making wax plates as carried out in this laboratory has been fully described by Dr. Florence R. Sabin.¹ A magnification of twenty diameters was decided upon, because (1) it gives a plate of convenient size to work with so that the numerous foldings of the surface of the dentate nucleus can be distinctly outlined, and (2) the thickness of the plates—2.8 mm.—makes them easy to cut and convenient to handle—two points of considerable practical value. Outline drawings were made first with a projection apparatus at a magnification of twenty diameters. These drawings were then controlled with a higher magnification before transferring them to wax plates.

In building the model a real difficulty presented itself—the

¹ Sabin, Contributions to the Science of Medicine, and Johns Hopkins Hospital Reports, ix.

difficulty of controlling the curves. Inasmuch as the central nuclei of the cerebellum lie deeply buried in the white matter of the hemispheres and worm one does not have the assistance afforded by external form in building up the model. In studying the sections it was noted that the dentate nucleus and accessory nuclei are bisymmetrical, and a prolongation of the raphe of the medulla dorsalwards bisected the cerebellum, passing through the middle point in the roof of the fourth ventricle. Corresponding points in the nuclei of the two hemispheres were equidistant from the median line so drawn and from the middle point in the floor of the fourth ventricle. In building the model these two guides were used: (1) the median line which controlled the lateral curve, and

to the lowermost (distal) section, in which the dentate nucleus appeared, was placed at a proper distance from the median line, *i. e.* the edge of the board and the upright outline of the floor of the fourth ventricle, and fixed in place. The succeeding plates were piled with reference to these two guides and the plates already piled, and each plate as it was put in proper position was fused with the plates already fixed.

The outline of the nucleus dentatus is very definite and easily traced. The capsule or Vleiss (Stilling) on the outside and the core or Markkern on the inside are both medullated and take the stain, thus distinctly limiting the yellow mass of cells composing the nucleus. The drawings could be very accurately made. In attempting to outline the accessory

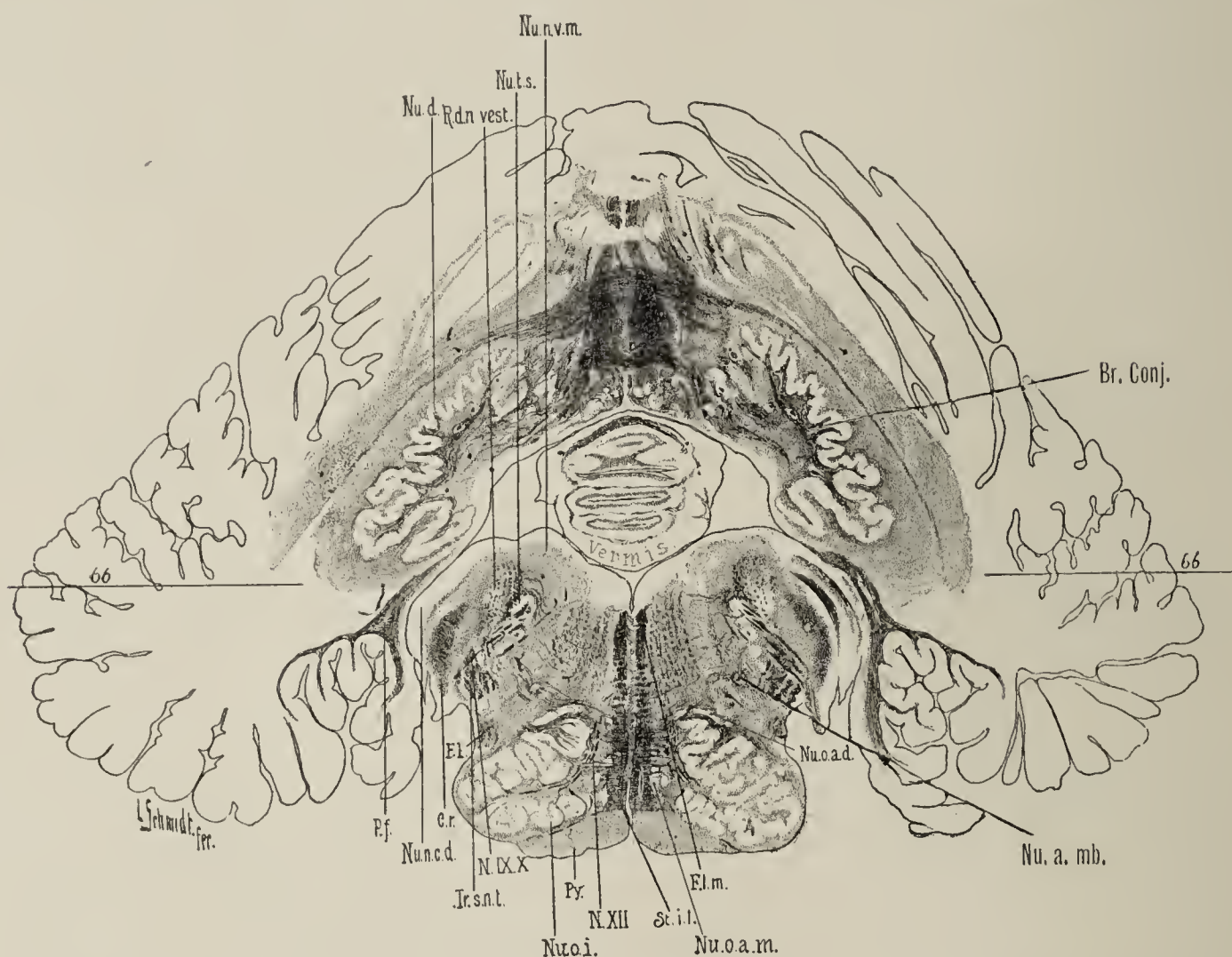


FIG. 1.—Transverse section of medulla and cerebellum (after Sabin, J. H. H. B., No. 81, December, 1897, Fig. 2.) Section at level of nucleus of glossopharyngeus and vagus nerves. Section also passes through upper part of the dentate nucleus and accessory nuclei. Long axis of nucleus is seen to form an acute angle, with the median line (formed by extension dorsally of the raphe bisecting the 4th ventricle and the cerebellum), with the angle opening toward the medulla. Dorsolateral surface of dentate nucleus is parallel to the surface of cerebellum. Corpus restiforme is seen to cover this surface. The accessory nuclei appear separated and broken up by the white medullated fibres. Variations in thickness and foldings of walls of the dentate nucleus also well shown. Hilus opens medial- and ventralwards.

(2) the outline of the floor of the fourth ventricle which controlled the dorsoventral curve. In the sagittal series the section passing through this central point in the floor of the fourth ventricle was selected and an outline of the longitudinal curve of the floor was made. A flat surface having one straight edge was then obtained. This edge corresponded to the median line. To this edge was attached the outline of the floor of the fourth ventricle, already described, at the proper angle corresponding to the angle at which the sections were cut. With these two guides fixed the plate corresponding

nuclei, however, one meets with a real difficulty. This applies particularly to the nucleus globosus and the nucleus of the roof. The nucleus globosus instead of forming one mass of gray matter is made up of several irregular groups of cells separated by deeply stained medullated fibres belonging to the fibre systems of this region. These separate groups are clearly limited with a magnification of twenty diameters, but when studied under higher powers one finds cells evidently belonging to these groups scattered among the dense network of deeply stained fibres. In studying the nucleus globosus

through several consecutive sections under high powers one gets the impression that the separate groups seen with a magnification of twenty diameters really form one nucleus; that this large mass of cells is separated into groups by the white fibres plunging directly through the nucleus; and this impression is further strengthened by noting the cells scattered among the fibres, included as it were by the bands of white fibres.

In outlining the nucleus of the roof one meets with the same difficulty. In going over these two nuclei with a high power to correct the drawings for transference to wax I had to include the scattered cells referred to. I did this by making the nuclei solid, not attempting to indicate the space occupied by the fibres.

One other point is to be noted. The so-called accessory nuclei, *i. e.* N. emboliformis, N. globosus and nucleus of the roof, are usually described and figured as entirely separate and distinct cell-mass. In this series of sections of the newborn babe, with the exception of the N. emboliformis, it has been difficult, indeed impossible, at certain levels, to separate these nuclei. The N. emboliformis forms a perfectly definite cell-group, in the lower (distal) sections, appearing as a thin, tongue-like ribbon of cells almost entirely occluding the hilus of the corpus dentatum. Sections at the level of the middle of the nucleus show it changing its shape, suddenly becoming thicker and shorter, but clearly separated from the corpus dentatum on one side and the nucleus globosus on the other side by thin, deeply stained bands of white fibres. The nucleus globosus also appears as a definitely limited and separate group of cells in the lower (distal) sections, appearing in sections a little above the beginning of the hilus of the corpus dentatum as a small oval area of gray matter. At a higher (proximal) level this oval mass is divided, as already indicated. At the highest levels it is not to be separated from the nucleus of the roof.

Corpus Dentatum.—It is embedded in the cerebellar hemisphere "like a peach stone" (Stillings). The distal end lies more deeply buried in the white substance; the proximal end approaches closely to the roof of the fourth ventricle, from which it is separated by a thin ribbon of white substance. Horizontal sections of the nucleus, as pointed out by Obersteiner, do not show the greatest diameter of the nucleus. This appears in sagittal sections.

The dimensions of the model of dentate nucleus are as follows:

1. Proximo-distal (sagittal), 19.8 cm.
2. Mesolateral, (in axis of nucleus and not at right angles to median line), 19.4 cm.
3. Dorsolateral, (perpendicular to mesolateral axis), 7.8 cm.

Remembering that the longest mesolateral diameter forms an acute angle with the median line with the angle opening ventralwards one will understand the measurements given.

The nucleus dentatus is really a hollow shell or sac with its long axis directed antero-posteriorly (proximo-distally). This shell is flattened dorsoventrally or at right angles to its mesolateral diameter. The walls, which vary in thickness

from 0.3 to 0.5 mm., are thrown into numerous folds also varying in number and size in different parts of the nucleus. The folding of the walls gives to the surface an appearance not unlike the surface of the cerebral hemispheres or to the gyri and sulci of the inferior olive. The shell of gray matter is not closed but freely opens above (proximally), while the ventral and mesial walls are incomplete in the anterior (proximal) two-thirds of the nucleus. This opening in the walls forming the so-called hilus—hilus corporis dentati—looks median-, ventral- and cerebralwards. In the distal one-third of the nucleus the walls are complete and in transverse sections appear as oval closed rings or ring of gray matter.

The hilus in the more distal sections opens directly medianwards; in sections at a higher level (cerebralwards) the opening increases rapidly in size, the ventral wall becoming less complete, while the dorsal wall forms a complete covering. As a result of this progressive shortening of the ventromesial wall the hilus comes to open wider and wider ventralwards. This direction is further emphasized by the relation of the nucleus emboliformis. In the most distal sections lying within the mouth of the hilus it is in very close relation with the dorsolateral border, indeed in the distal sections it may be considered as a continuation of the dorsolateral surface on to the mesial surface, being separated by a very thin band of white fibres. This relation continues throughout the entire length of the nucleus, there being only a thin space of separation through which pass the most dorsal fibres escaping from the Markkern of the nucleus dentatus.

In addition, the dentate nucleus presents for description two surfaces, (1) dorsolateral, and (2) ventromesial; and four borders, (1) mesial, (2) lateral, (3) proximal, and (4) distal.

Dorsolateral Surface.—This is the largest surface of the nucleus (Fig. 2). It is irregularly quadrilateral in shape and lies parallel to the surface of the cerebellar hemisphere. The lateral and antero-posterior (proximo-distal) curves are slight, the surface being quite flat. In this connection it is interesting to note that a portion of the corpus restiforme lies over this surface of the nucleus, forming a shell enclosing the dorsolateral surface. This surface terminates mesially by a sharp thin border in its upper (proximal) two-thirds, by a rounded mesial border in its lower (distal) one-third. Laterally it is limited by the thicker, irregular and rounded lateral border. The proximal border also thin forms with the median line an obtuse angle opening spinalwards. The distal border is parallel to the proximal, is thick, rounded and is broken into by deep sulci. By reference to Fig. 2 it will be seen that the lowest sections of the nucleus includes only the mesial portion of this border.

The dorsolateral surface is traversed by five parallel deep fissures, which run parallel to the long axis of the nucleus. Beginning with median line these may be designated as A, B, C, D and E. These fissures divide the surface into six columns or gyri. Besides these five primary fissures there are five secondary sulci, which are shallower and incompletely divide the primary columns or gyri into secondary gyri. By reference to Fig. 2 the following points will be noted: Fissure

A is parallel to the mesial border, it is relatively deep and its corresponding gyrus on the inner surface of the nucleus looks lateralward (Fig. 3). The proximal end of fissure *A* curves laterally. Fissures *B* and *C* present three curves, the proximal and distal with convexities pointing mesially, the middle with convexity laterally. Fissure *C* is incomplete, its proximal end not reaching the proximal border. Fissures *D* and *E* form acute angles with fissure *C* with their proximal ends pointing obliquely medialwards. It will also be noted that the distal extremities of the columns or gyri are larger, thicker and divided by extension on to this surface of the fissures from the ventromesial surface. The deep fissures of the ventromesial surface alternate with the fissures on the dorsolateral surface. An exception to this is in fissure *D*, which is really an extension on to the dorsolateral surface of the lateral fissure of the ventromesial surface. There is no evidence of distinct lobulation visible on this surface.

The secondary sulci are limited chiefly to the three gyri nearest the median line. In other words, the folding of the dorsal wall of the nucleus is greatest nearer the mesial and proximal borders; it is thickest nearer the lateral and distal borders.

Ventrolateral Surface.—This surface is incomplete in its upper two-thirds. It differs markedly from the dorsolateral surface. It presents two deep fissures radiating from a point near the hilus about the level of the middle point of the nucleus. These fissures may be designated as (1) internal and (2) lateral. Within the internal fissure and nearly covered over by its projecting edges is a gyrus, broad at its base (distal end) and tapering above, becoming lost in the most proximal part of the fissure. This gyrus, partly concealed within the internal fissure, divides this fissure into two, both of which extend so as to appear on the dorsolateral surface. These two fissures, internal and lateral, of the ventromesial surface, divide this surface into three lobes, (1) internal, (2) median, and (3) lateral. The internal is the smallest and continues below the hilus on to the mesial border, being distinctly marked off from this border by a shallow sulcus. This lobe is broad at its proximal end, tapering off distally. The median lobe, broad at its base—distal end—narrows toward the point of divergence of the two fissures, internal and lateral. The internal and median lobes form the most distal part of the nucleus as viewed from its ventral aspect. They slope with a considerable curve to meet the almost perpendicular dorsolateral surface. They present no secondary sulci.

The lateral lobe is the largest. It forms the lateral border and extends on to both dorsolateral and ventromesial surfaces. On the former it lies lateral to fissure *E*, while on the latter it is limited mesially by the lateral fissure. This lobe is most irregular in outline, is broken up by numerous depressions and several secondary sulci. One of these sulci, more conspicuous than the others, runs parallel to the upper two-thirds of the lateral border.

The upper two-thirds of the ventromesial border is incomplete; the margin is very irregular as will best be understood

by reference to Fig. 3. In general, it may be said that this surface, as compared with the dorsolateral, presents (1) deeper fissures, which give the appearance of lobulation, (2) thicker walls, and (3) fewer foldings of the walls.

The proximal end of the nucleus being open this border is limited to the thin edge of the dorsolateral surface, and the very small part of the ventromesial surface. This border slants obliquely spinal- and medianwards. The other borders have been referred to in describing the surfaces and the hilus.

The Accessory Nuclei.—The form and outline of the accessory nuclei, *i. e.* the nucleus emboliformis, nucleus globosus and nucleus of the roof, have been already referred to. Figs. 5, 6 and 7 show these nuclei in relation to the dentate nucleus. In Figs. 5 and 7 the nucleus emboliformis is seen as a long thin sheet of gray matter separated from the dorsolateral surface of the nucleus dentatus by a narrow space already described. Its most distal end nearly occludes the hilus corporis dentati (Fig. 7), while proximally it changes its form, becoming thicker and shorter, encroaching less on the hilus. It will also be noted (Fig. 5) that its axis changes; at first running dorsoventrally in its distal extremity, it comes to lie more laterally in its proximal part, corresponding in direction with the dorsolateral wall of the dentate nucleus. This nucleus is practically separate throughout its entire length, being the most definitely outlined of the accessory nuclei.

The nucleus globosus (Fig. 5) is also seen as a distinct oval mass of gray matter in its distal portion, beginning a little above the appearance of the hilus. In its proximal end this nucleus is represented as fused with the nucleus of the roof (Figs. 5 and 7).

The nucleus of the roof appears in the reconstruction as a large irregular mass, distinct in its distal portion, becoming fused with the nucleus globosus in its proximal portion. The outlines of this nucleus are indefinite in this series, its ventral surface being in very close relation with the gray matter of the roof of the fourth ventricle.

DESCRIPTION OF PLATES XXIX-XXX.

FIG. 2.—View of dorso-lateral surface of model of *N. dentatus*. Proximal end corresponds to top of figure; median line is to left. *M*, mesial border; *T*, lateral border; *A*, *B*, *C*, *D*, *E*, are placed over primary fissures; *a*, *b*, *c*, *d*, *e*, over secondary sulci; *f*, is extension on to dorsolateral surface of the internal fissure of the ventromesial surface.

FIG. 3.—View of ventromesial surface of model of *N. dentatus*. Median line to right. *I*, internal fissure; *L*, lateral fissure; *i*, internal lobe; *m*, median lobe; *l*, lateral lobe; *H*, hilus.

FIG. 4.—View of mesial border of same at right angles to median line. Relations of hilus to dorsolateral and ventromesial walls are shown. Distally the hilus is narrow, increasing rapidly as one passes cerebrolwards.

FIG. 5.—View of mesial border of *N. dentatus* with accessory nuclei in place.

S, nucleus emboliformis; *G*, nucleus globosus; *R*, nucleus of the roof; *o*, narrow space through which escapes most dorsal fibres from Markkern.

FIG. 6.—View of dorsolateral surface of same. Legend as in Figs 2 and 5.

FIG. 7.—View of ventromesial surface of same. Legend as in Figs 3 and 5.



FIG. 2.

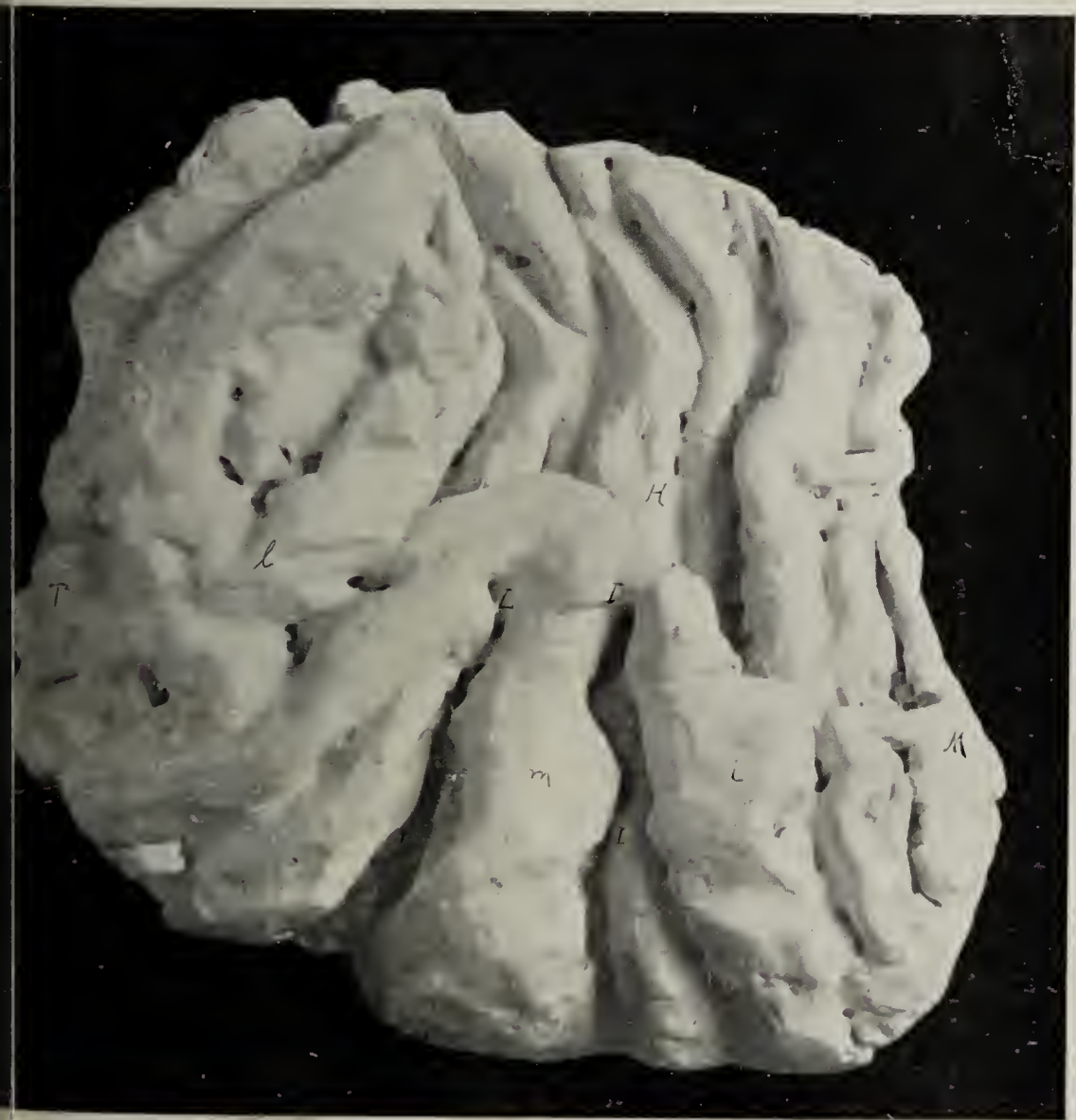


FIG. 3.

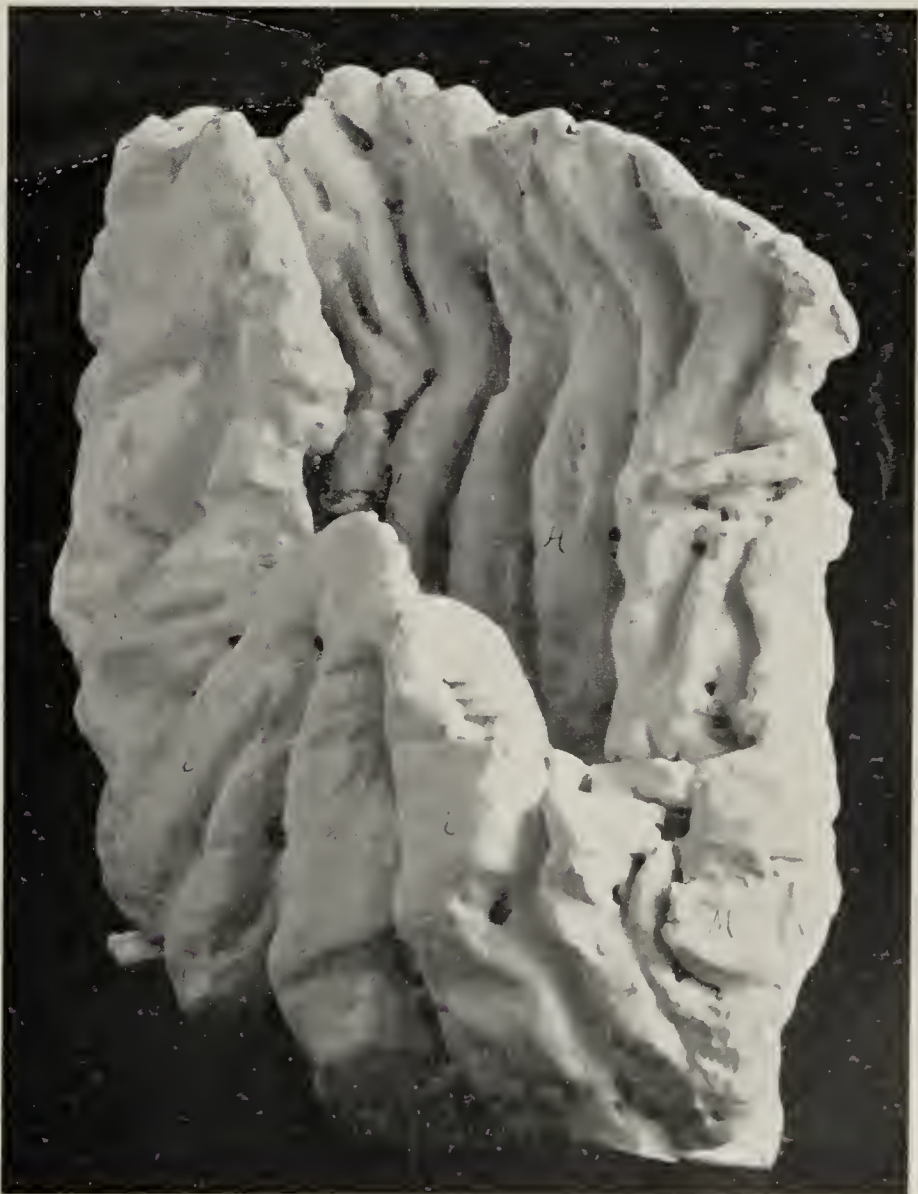


FIG. 4.



FIG. 5.

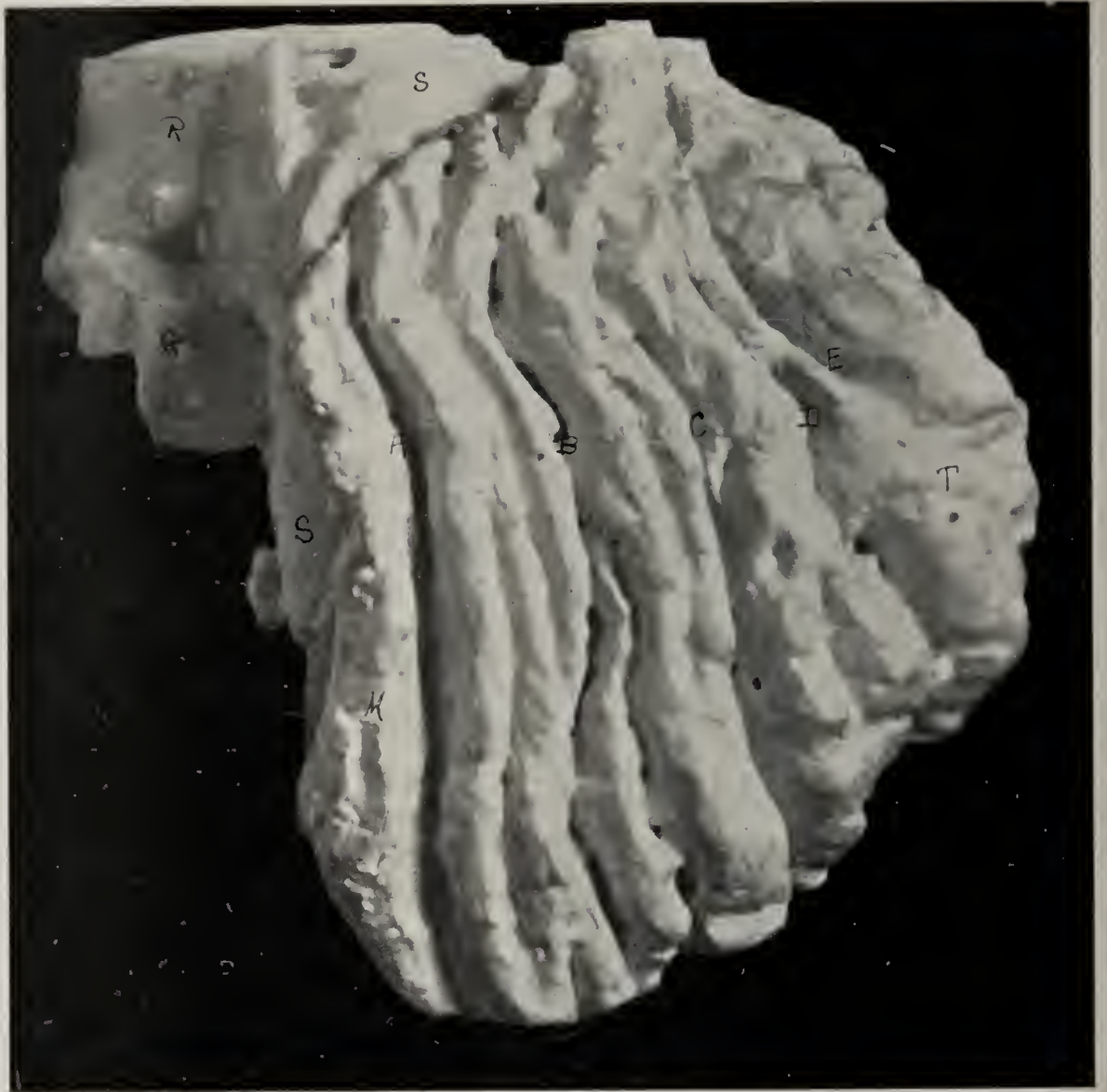


FIG. 6.



FIG. 7.

USE OF THE MATERIAL OF THE DISSECTING ROOM FOR SCIENTIFIC PURPOSES.

BY CHARLES RUSSELL BARDEEN, M. D.,
Associate in Anatomy, Johns Hopkins University.

Rosenberg, in a recent article,¹ has called attention to the opportunities that the dissecting room offers for scientific investigation. He gives an interesting summary of the various attempts that have been made to take advantage of these opportunities, and calls particular attention to the records obtained by Schwalbe at Strassburg, by Cunningham at Dublin, and by the Anatomical Society of Great Britain and Ireland.

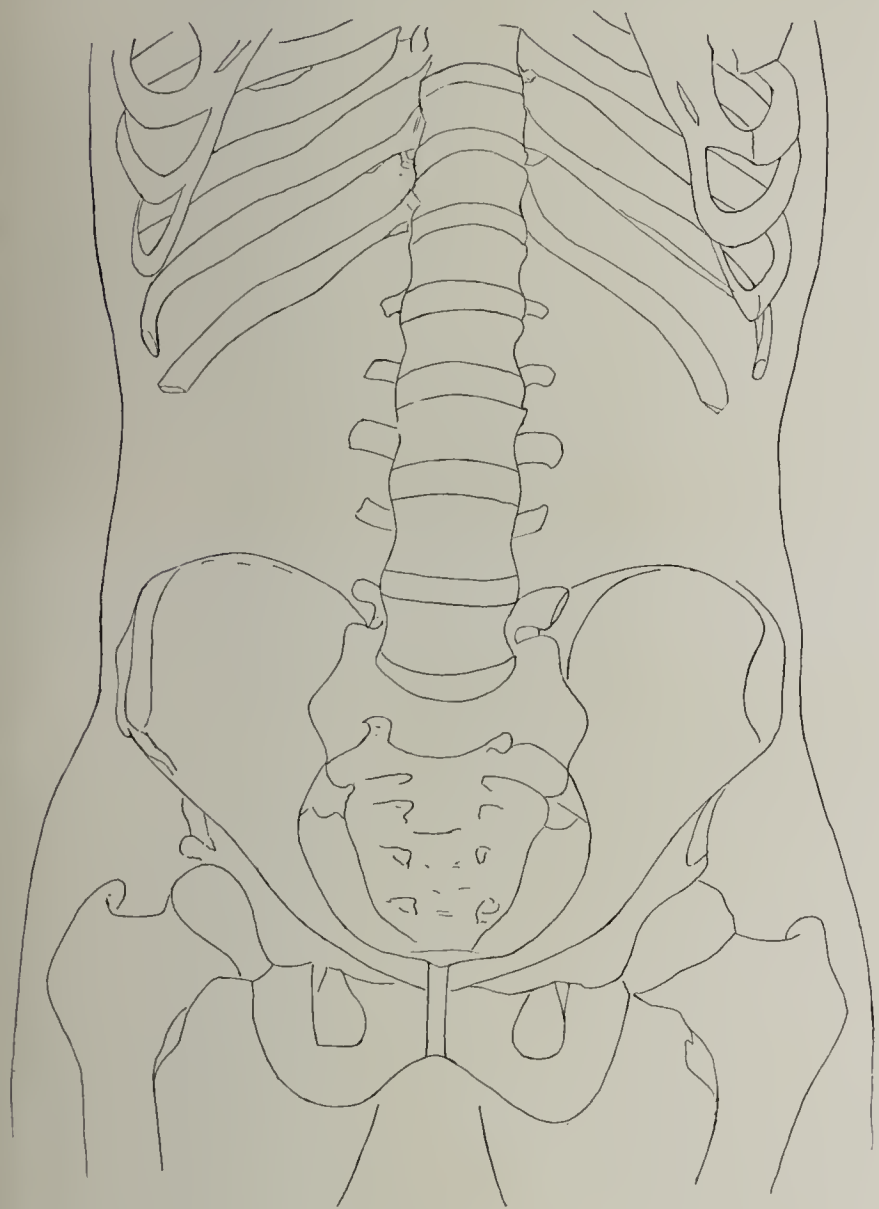


FIG. 1.

It has seemed to me that the methods employed to utilize the material of the dissecting room and the work of the students for scientific purposes in Professor Mall's laboratory at the Johns Hopkins University, Baltimore, may prove of interest, possibly of value, to those engaged elsewhere in anatomical instruction.

The immense amount of study that has been given to the structure of the human body during the last four centuries renders it unlikely that the student's untrained eye and hand could be utilized to advantage in a search for unrecorded

facts of gross structure even if time permitted him to delve in those little nooks and corners where the records are still incomplete. The very considerable amount of variation, however, which the individual bodies present in the structure, form and relationships of their various organs, offers a rich field for cultivation.

Since the time of Darwin much attention has been given to the study of variations in plants and animals. The greater part of the attention, however, has been given to external features, to variation in size, color, and external form. Few studies have been made of the frequency of variation in the internal organs. Yet probably the body of no animal is more suited to this study than that of man and none is studied with care by so great a number of individuals each year.

Until comparatively recently the variations brought to light by the dissector have been recorded only when of an unusual nature. These observations, however, have been so numerous that we may assume that most of the variations likely to be brought to light have previously been recorded. While the limits of variation of the various organs of the body are thus fairly well understood, the frequency of variations has been determined but for few organs and for them only incompletely. The true "normal" or "most usual" is unknown. Henle, in his anatomy, pictured that as normal which his experience led him to think the most usual. Most of the other leading anatomists have done likewise. No two books, other than compilations from similar sources, give the same account of the normal form of the various organs. The great opportunity which the dissecting room offers is that of determining the curve of frequency of the various forms presented by bodily structures, and thus to make the normal a question of measurement rather than one of judgment. To render this possible, accurate records of the conditions found in each body must be made, of such a nature that they may be afterwards compared and reduced to tables.

The method of record thus becomes a question of paramount importance.

In the Anatomical Laboratory at the Johns Hopkins University the first attempts at making systematic records of conditions of structure revealed at the dissecting table were begun in the fall of 1895. It was determined to make a study of the variations in the distribution of the cranial and spinal nerves, especial attention being paid to the cervico-brachial and the lumbosacral plexuses. At the instigation of Professor Mall, Dr. A. W. Flting, at that time Assistant in Anatomy, prepared three record-charts, one for the nerves of the head, one for the nerves of the neck, arm and upper half of the thorax, and one for the lower half of the body. On these charts a record was made of the sex, color, and age

¹ *Morphologisches Jahrbuch*, 1895.

as well as of the nerve distribution in the body of the individual dissected. The scheme for recording the latter was as follows. On separate successive lines the numerical designation of a given cranial or spinal nerve was placed, followed by a list of the names of the nerves to which the given main nerve trunk was assumed to contribute. In the preparation of this table the standard anatomies were consulted. A few

The students were requested to compare carefully the nerves in the part dissected with the outline scheme, to underline the names of those nerves which were found to correspond with the scheme, to cross out the names of the nerves which did not thus correspond, and to insert these names in the proper place. Complex conditions, such for instance as are found in the cervicobrachial and the lumbo-

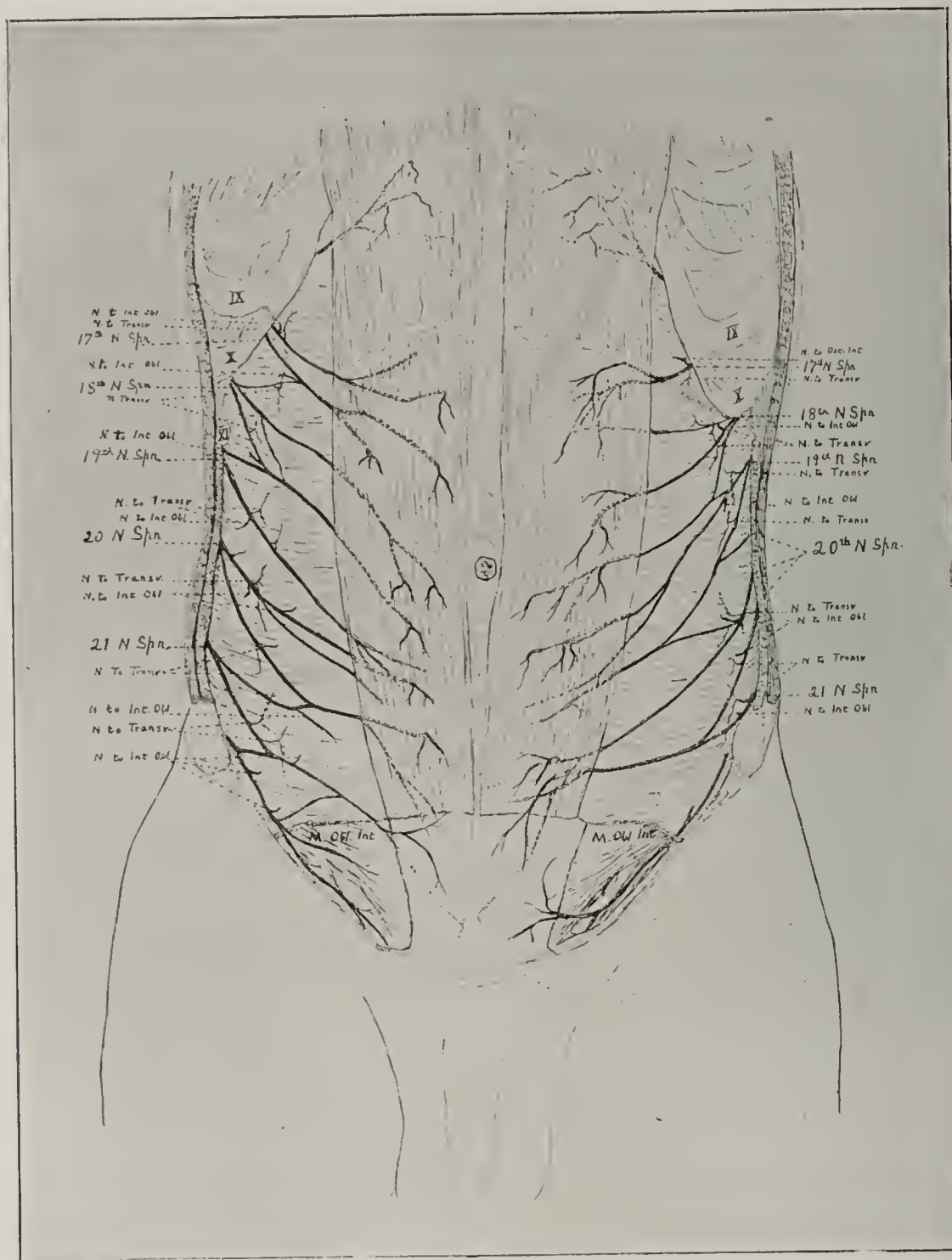


FIG. 2.

lines from the "Cervicobrachial Chart" may suffice to make clear the general nature of this scheme:

C. VI. POST-BR. ANT-BR.—POST-THORACIC. SUBCLAVIUS. SUPRASCAP. COM. **C. VII.**

C. VII. POST-BR. ANT-BR.—EXT-ANT-THORACIC. COM-POST. CORD. Outer Cord. MUSC-CUT.—Cor-brach. Biceps. Br-ant. Ant. Post. OUTER-HEAD-MEDIAN.—Ant-interos. Palm-cut. Thumb-br. 5 Digitals.

C. VIII. POST-BR. ANT-BR. Inner Cord. Post. Cord. SUBSCAPS.—Upper. Middle. Lower. CIRCUMFLEX.—Sup. Inf. Art. MUSC. SPIRAL.—Musc. Int-cut. Ext-up-cut-br. Ext-low-cut-br. Musc. RADIAL.—Ext-br. Int-brs. 4. POST-INTEROS.—Musc. Art. COM. **D. I.**

sacral plexuses, were illustrated by diagrams drawn on the backs of the charts.

These outline schemes were well arranged and theoretically should have worked well. Yet they did not prove a success in the hands of the students. The suggestion induced by print seemed continually to lead the student into reading the scheme into his "part." The task of verifying the charts thus became a severe one. Another difficulty came from the fact that names can mean little so long as the "normal" is unknown. While the larger nerves are so constant in position that the names current in the text-books

could be used without confusion it was found that many of the smaller nerves could be definitely recorded only by attaching a special definition to the name. The *iliohypogastric* and the *genitocrural* nerves may be mentioned as examples. The value of these earlier charts lies rather in the illustrative diagrams of the plexuses placed on the backs of the charts than in the records made on the tabulation schemes.

In the fall of 1897 I undertook the immediate supervision of these records. I discarded to a considerable extent the use of the printed schemes. The students were encouraged to record the distribution of the nerves by making free-hand

of the front of the thigh; one for the sacral plexus; one for the perineum; one for the back of the thigh, etc., in all 26 charts.² Separate charts are used for the right and left sides of the body.

In these diagrams the bones and the surface outline of the body after the removal of the skin and the superficial fascia are indicated by fine lines printed in brown ink. The scale of the charts varies from one-half to full life size, according to the region to be charted. In this way the general average proportions of the various parts of the body are furnished the student. Marked variations from these proportions can

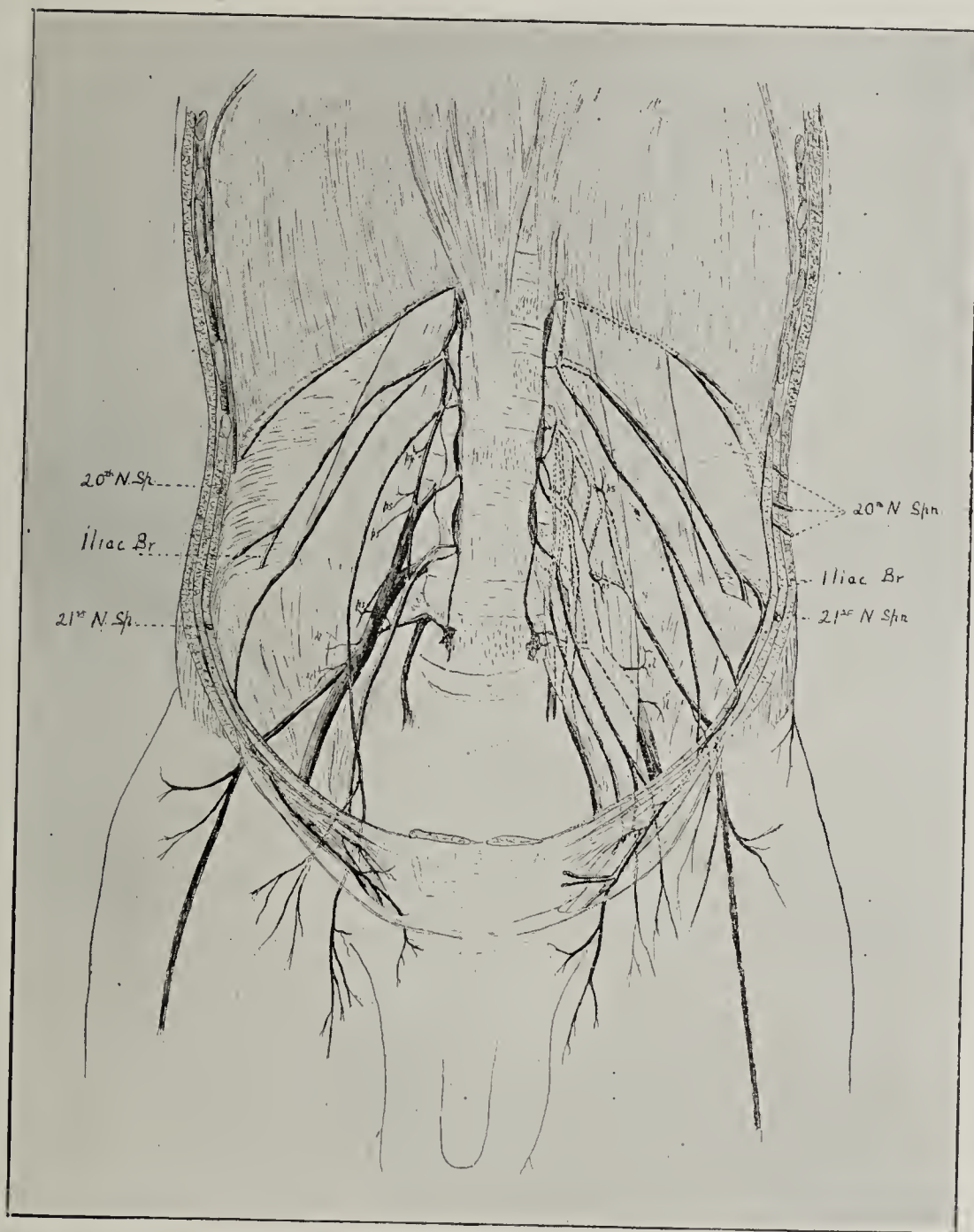


FIG. 3.

diagrammatic sketches to illustrate the conditions found in the parts dissected. Many of the drawings thus made were well executed. Yet few of the students are sufficiently skillful draughtsmen to make even these simple sketches without a great expenditure of time. I therefore devised a set of simple outline diagrams on which the nerve distribution can be recorded. These diagrams are arranged for the various parts of the body. Thus there is one for the abdomen, which can be used either for the nerves of the abdominal walls or for the lumbar plexus (see Figs. 1-3); another for the nerves

readily be indicated by changing the faint outlines of the skeletal scheme. After removing the skin from a given part of the body the student draws on the appropriate diagram the course of the superficial nerves as he finds them running in the fascia. When the muscles have been dissected out the nerve supply of the various muscles is charted. Muscles and other structures are drawn in to show the general relations of

² These charts have been published in pamphlet form: "Outline Record Charts." The Johns Hopkins Press, Baltimore, 1900.

the nerves. The best records have been obtained when the student has attempted to record only a few simple conditions on a single chart. Thus in charting the nerves of the front of the thigh separate charts are used to record the distribu-

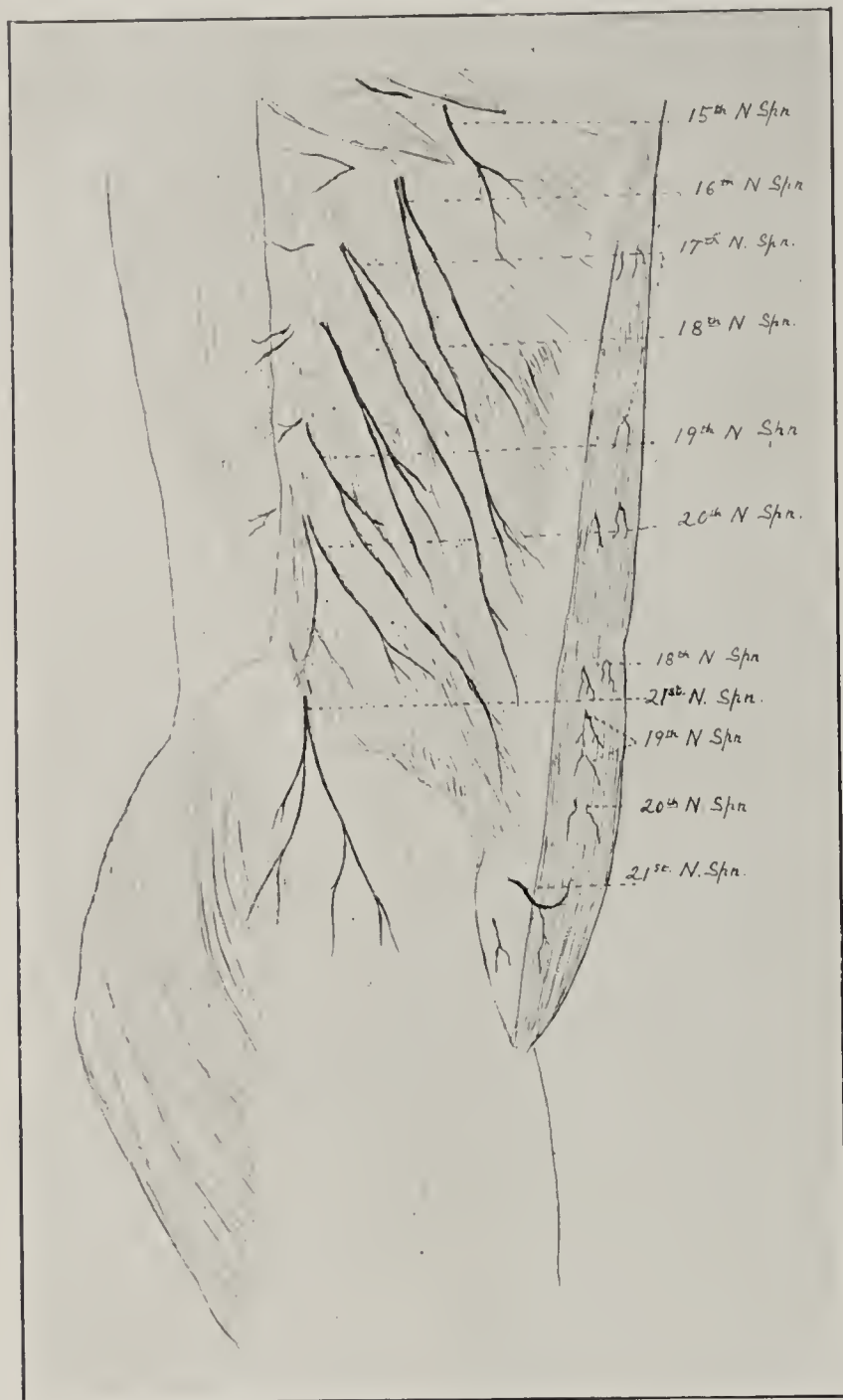


FIG. 4.

tion to the *sartorius* muscle, to the *rectus* muscle, to the *deep extensor* muscles, to the *adductor longus* muscle and the *gracilis*, to the *adductor brevis* muscle, and to the *adductor magnus* and *external obturator* muscles.

To illustrate the method of using these charts a few ex-

amples may be given. Fig. 1 represents the outline diagram used for the abdomen and the lumbar region. Fig. 2 shows the distribution of the main ventral trunks of the abdominal nerves as dissected out and recorded by two students. Fig. 3 represents the lumbar plexuses and the distribution of the "border nerves" found in the same subject. The lateral branches of the abdominal nerves are shown in another chart (Fig. 4).

Of course one cannot hope to get from students the complete and accurate records which one could get by personal dissection. It is only rarely that perfectly satisfactory records are obtained of the peripheral distribution of all the nerves. On the other hand, it would be a physical impossibility by personal dissection to get the same number of records in the same space of time. Mistakes are more likely to be those of omission than of a positive nature. The student may destroy some fine nerve twig before it has been seen by an instructor, and thus it may escape record. The conditions that the average student finds and records are, however, of great value. Thus only may we hope to get that large number of records from which a curve of frequency may be determined.

In addition to the outline diagrams I have devised a simple printed scheme for keeping record of the race, sex, age, size, skeletal peculiarities and marked variations from the normal in the various organs of the body. This latter set of records is made out by the instructor who verifies the charts.

The verification of the charts is one of the most important features of the undertaking. Without careful verification by one man who gives his time in the dissecting room mainly, if not wholly, to this task the charts can be of little value.

Active co-operation on the part of all the instructors and of the students in the dissecting room is also essential.

The conditions which at present prevail in our medical department render it also perhaps more than usually easy to get the co-operation of the students in carrying out work of this kind. The standards of admission to this school bring us a much more highly trained class of students than those usually found entering the average American medical school. On the other hand, the routine of a graded course, while inferior as a method of education to that freedom of choice which marks the German university, renders it much easier to win the co-operation of the students in this work. The number of students dissecting each year since the beginning of the undertaking has averaged about one hundred.

ON THE DEVELOPMENT OF THE HUMAN DIAPHRAGM.

BY FRANKLIN P. MALL,

Professor of Anatomy, Johns Hopkins University.

In a paper on the development of the human coelom, published several years ago, I was not able to give a detailed description of the separation of the body cavities from one

another, because the specimens at my disposal did not include all the necessary stages. For that study I used 19 human embryos between 2 and 24 mm. long, in which various stages of the development of the body-cavities were shown, but a number of the important stages were missing.

¹ Mall, Jour. of Morph., vol. 12, 1897.

During the past three years the collection of human embryos in the anatomical laboratory has grown very rapidly and all the missing stages for the study of the formation of the body-cavities have been supplied. The following table gives a list of these embryos. It will be seen from it that

TABLE OF EMBRYOS.

No.	Greatest length in mm.	Time between the beginning of the last period and the abortion.	Direction of the section.	From whom obtained.
XII.	2.1	41 days	Transverse	Dr. Ellis, Elkton, Md.
CLXIV ...	3.5	...	"	Dr. MacCallum, Baltimore.
CXLVIII .	4.3	38 days	"	Dr. Hoen, Baltimore.
LXXVI ...	4.5	...	"	Dr. Mitchell, Chicago.
LXXX ...	5	...	"	Dr. Branham, Baltimore.
CXXXVI .	5	56 days	Sagittal	Dr. Campbell, Halifax, N. S.
CXVI	6.5	55 days	"	Dr. Ryan, Springfield, Ill.
II.	7	52 days	Transverse	Dr. C. O. Miller, Baltimore.
CXIII	8	...	Sagittal	Dr. Gray, Washington.
CLXIII ..	9	5 weeks	Transverse	Dr. Lamb, Washington.
CXIV	10	...	Sagittal	Dr. Gray, Washington.
CIX.	11	...	Transverse	Dr. Cushing, Baltimore.
CXLIV ...	14	...	Sagittal	Dr. Watson, Baltimore.
XLIII	16	...	"	Dr. Booker, Baltimore.
LXXIV ...	19	...	Transverse	Dr. Irving Miller, Baltimore.

the series from 2 mm. upward is very complete with the exception of stages between 11 and 14 mm. long. Fortunately, the missing stages are not important. All the embryos given in this table are practically perfect, the imperfect ones having been excluded. The present study is based upon 15 embryos, only 3 of which are included in the 19 specimens considered in the earlier communication.

It has often been stated that the development of the diaphragm, especially in the human embryo, is one of the most difficult problems of embryology, partly because of the difficulty in obtaining the necessary specimens and partly because there are no fixed points from which to calculate. In its development the whole diaphragm wanders from the head to the abdomen, passing by as well as modifying the structures and organs along the way. So, while von Baer recognized that the diaphragm wandered in its development, picking up its nerve in so doing, a fairly clear picture of the whole process was not given until His studied carefully the development of the neck, heart, lungs and intestine. In his studies His recognized the *Anlage* of the diaphragm in a mass of tissue located with the heart amongst structures belonging to the head and containing within it the veins to the heart as well as the *Anlage* of the liver. This mass of tissue His termed the septum transversum. His studies

were made upon the human embryo, mainly by the method of reconstruction, and shortly after they were published Uskow made a very careful study of the further growth of the septum transversum. Uskow recognized the great importance of two additional structures in the formation of the pericardium and adult diaphragm from the septum transversum; these he termed the *pleuro-pericardial membrane*, containing the phrenic nerve, and the *pillars* which form the dorsal ends of the diaphragm. The pillars of Uskow have been termed the *pleuro-peritoneal membranes* by Brachet, and as the latter term is more appropriate than the former I shall employ it in the present paper.

My own studies show that the pleuro-pericardial and pleuro-peritoneal membranes arise from a common structure, which extends from the lobe of the liver along the dorsal wall of the ductus Cuvieri to the dorsal attachment of the mesocardium. Later this structure grows towards the head to complete the pleuro-pericardial membrane and then towards the tail to complete the pleuro-peritoneal membrane. This structure, which I shall term the *pulmonary ridge*, is located in the sagittal plane of the body-cavity with cephalic and caudal horns on its dorsal side. The ductus Cuvieri lies between these horns (Fig. 29).

The purpose of this paper is to follow carefully the fate of the septum transversum and the origin and fate of the pulmonary ridge in the human embryo. In so doing it is of course necessary to consider the division of the body-cavity into the pericardial, pleural and peritoneal cavities. According to His, the body-cavity in early embryos is divided into the *Parietalhöhle* and *Rumpfhöhlen*. The communication between these spaces he has also termed the recessus parietalis. The parietal cavity from its earliest appearance contains the heart and is destined to form the pericardial cavity. I shall term it the pericardial coelom. A portion of the recessus parietalis forms the pleural cavity; it surrounds the lung bud throughout its development and I shall term it the pleural coelom. The remainder of the recessus parietalis to the origin of the liver has developed in it the liver and stomach; this is added to the general peritoneal cavity and I shall term it the peritoneal coelom. In the early embryos the whole coelom lies far out of place; in Embryo XII nearly the entire coelom lies in the region of the head and neck and in the further development of these parts the coelom with the surrounding organs wanders away from the head to its permanent location. As long as the serous cavities arising from the coelom are in the process of wandering and are not fully separated from one another I shall term them pleural, pericardial and peritoneal coelom; when they are fully established I shall call them cavities.

In Embryo XII, Fig. 1, the coelom of the embryo forms a free space encircling the heart and extending on either side of the body over the omphalo-mesenteric veins to the root of the umbilical vesicle. This canal of communication has developed within it the lung, stomach and liver, and throughout its earlier development it measures in length about one-fourth of that of the body (Embryos XII, CXLVIII, LXXVI,

LXXX. II and CLXIII). The appearance of the lung and liver marks the subdivision of the coelom into the pleural and peritoneal coelom. With the development of the liver, lung and stomach the coelom containing them gradually dilates until the embryo is about 9 mm. long, when the canal evaginates, so to speak, and turns the liver and stomach out into the general peritoneal cavity. The Wolffian body, which occupied the dorsal wall of this canal, gradually degenerates and the lung takes its place. From these statements it is readily inferred that the canal extending from the pericardial coelom, His's recessus parietalis, gives rise to the pleural coelom on its dorsal side and to the peritoneal coelom on its ventral side. The line of division is formed by the pleuro-peritoneal membrane extending from the ductus Cuvieri to the adrenal.

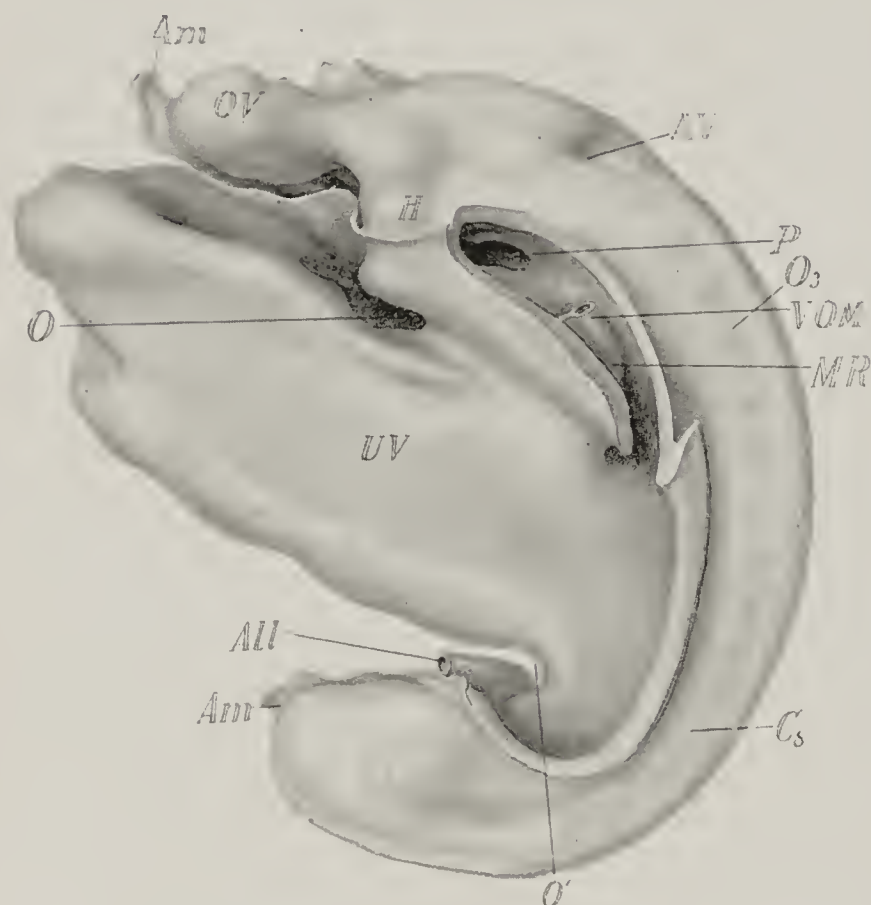


FIG. 1.—Profile reconstruction of the embryo 2.1 mm. long. No. XII $\times 37$ times; *am*, amnion; *ov*, optic vesicle; *av*, auditory; vesicle *uv*, umbilical vesicle; *h*, heart; *vom*, omphalo-mesenteric vein; *mr*, septum transversum; *o₃*, third occipital myotome; *c₈*, eighth cervical myotome.

The earliest embryo in my collection in which the septum transversum is well formed is No. XII, 2.1 mm. long, and about two weeks old.² The specimen is very valuable for the study of the beginning of so many structures that it also becomes a good starting point for the study of the development of the diaphragm.

Figs. 1 and 2 give the external form and outline of the neural tube and alimentary canal drawn from a reconstruction. It is seen that the coelom sends two canals into the

head on either side of the neck which communicate with each other in the immediate neighborhood of the mouth. This U-shaped canal is separated from the exocoelom on its ventral side by a bridge of mesodermal tissue connecting the umbilical vesicle with the embryo at the juncture of the head with the amnion. It follows that this bridge of mesodermal tissue, the septum transversum, is also U-shaped, as is shown in Figs. 1 and 2. *ST* and *MR*. It forms a portion of the ventral wall of the pericardial coelom and supports the omphalo-mesenteric and umbilical veins. Sections of it are shown in Figs. 3, 4 and 5, which are from three sections through the head end of this embryo in the neighborhood of the first cervical myotome. The *Anlage* of the liver is shown in Fig. 4, which is located in this stage in a region belonging to the head.

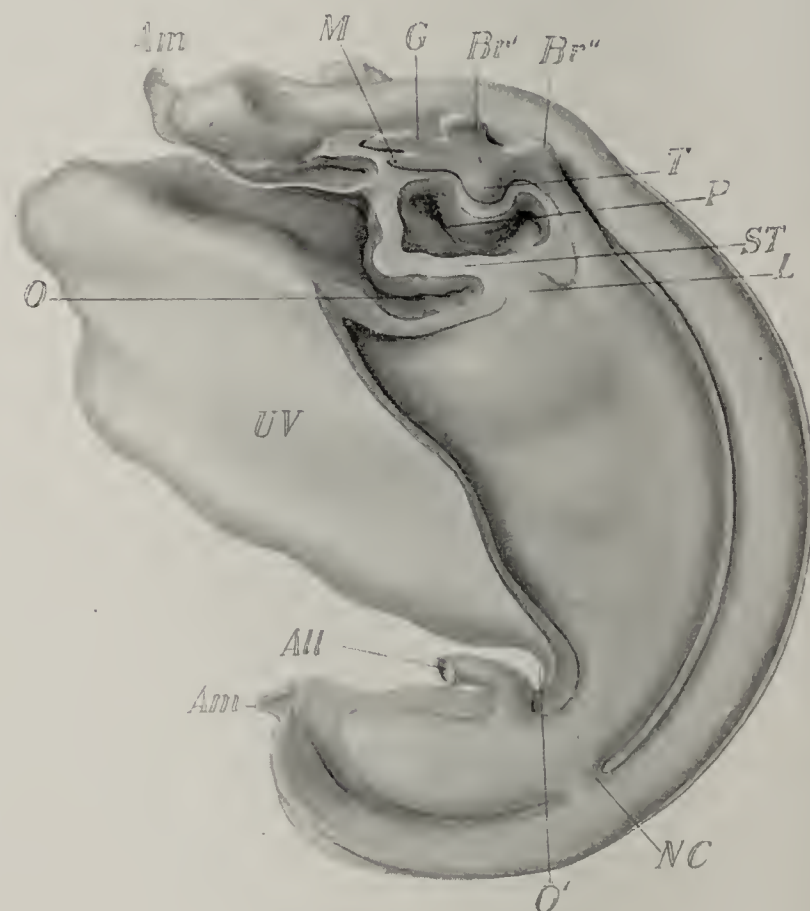


FIG. 2.—Partial dissection of the reconstruction of the embryo 2.1 mm. long. No. XII $\times 37$ times; *am*, amnion; *m*, mouth; *Br'*, *Br''*, first and second branchial pockets; *t*, thyroid; *p*, pericardial coelom; *st*, septum transversum; *l*, liver; *uv*, umbilical vesicle; *nc*, neurenteric canal.

Figs. 6 to 9 are from an embryo (CLXIV) slightly more advanced in development than No. XII. The embryo is from an ovum measuring 17 x 17 x 10 mm., found in the uterus at an autopsy. When the uterus was cut open the knife entered the ovum and possibly distorted the embryo, for when it came into my hands it was found that the embryo was floating in the cavity of the ovum but it was still adherent to its walls. This mechanical injury undoubtedly caused the body of the embryo to straighten and at the attachment of the umbilical vesicle the body of the embryo is bent towards the ventral side, as is the case in a number of the His embryos (for instance, BB). The ventral wall over the heart was also slightly torn. The entire uterus and ovum had been

² Different pictures of this embryo will be found in the Journal of Morph., vol. 12; His's Archiv, 1897; Johns Hopkins Hospital Bulletin, 1898; and the Welch Festschrift, Johns Hopkins Hospital Reports, vol. 9.

preserved on ice for 21 hours, and when it was given to me by Dr. MacCallum the entire specimen was placed in strong formalin. The sections of the embryo show that the tissues are slightly macerated but in general they are well preserved. The spinal cord is closed throughout its extent but the neuropore is still open. The thyroid gland, optic and otic

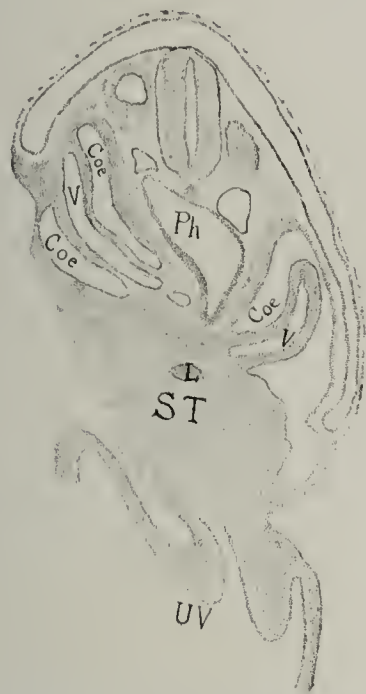


FIG. 3.—Section through the head of the embryo 2.1 mm. long. No. XII $\times 50$ times; *coe*, coelom; *ph*, pharynx; *l*, liver; *st*, septum transversum; *uv*, umbilical vesicle.

vesicles, heart and veins, are but slightly more developed than in No. XII. If this embryo were curled up as No. XII it would measure from 2.5 to 3 mm., while if the two had been hardened in the same way (No. XII was hardened in alcohol) they would probably measure alike.

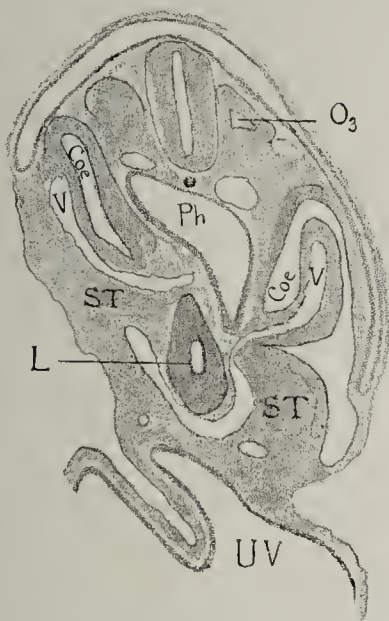


FIG. 4.—Section through the third occipital myotome of the embryo 2.1 mm. long. .04 mm. nearer the tail than Fig. 3 $\times 50$ times; *O₃*, third occipital myotome; *coe*, coelom; *v*, vein; *st*, septum transversum; *l*, liver; *ph*, pharynx; *uv*, umbilical vesicle.

The figures given show the general relation as seen in Embryo XII with each of the structures but slightly advanced. The septum transversum is much the same as it is in XII, while the pericardial coelom is pushed more to the ventral side of it and the diverticulum to form the liver is more marked. The umbilical vein has extended somewhat (Fig. 9) and the jugular vein has made its appearance (Fig. 7).

The tissue of the septum transversum in the two embryos is formed of irregular round cells, between which there are numerous vessels, of irregular diameter, which communicate freely with the veins to the heart.

The next stage of the development of the septum trans-

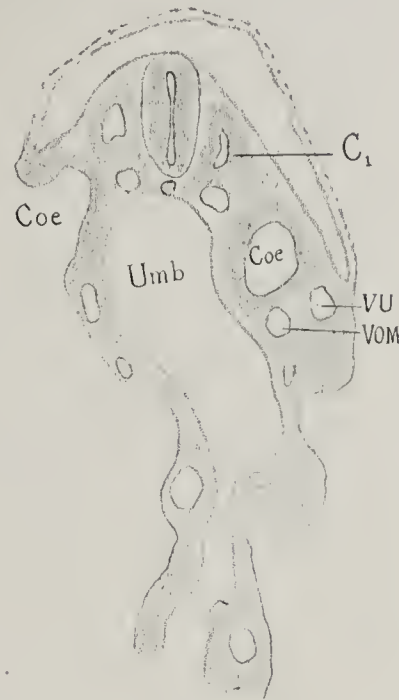


FIG. 5.—Section through the first cervical myotome of the embryo 2.1 mm. long, .23 mm. nearer the tail than Fig. 4 $\times 50$ times; *C₁*, first cervical myotome; *coe*, coelom; *vu*, umbilical vein; *vom*, omphalo-mesenteric vein; *umb*, umbilical vesicle.

versum is found in an embryo 4.3 mm. long (CXLVII), obtained from Dr. Hoen.³ The specimen is perfect and normal, as it was obtained through mechanical means. The entire

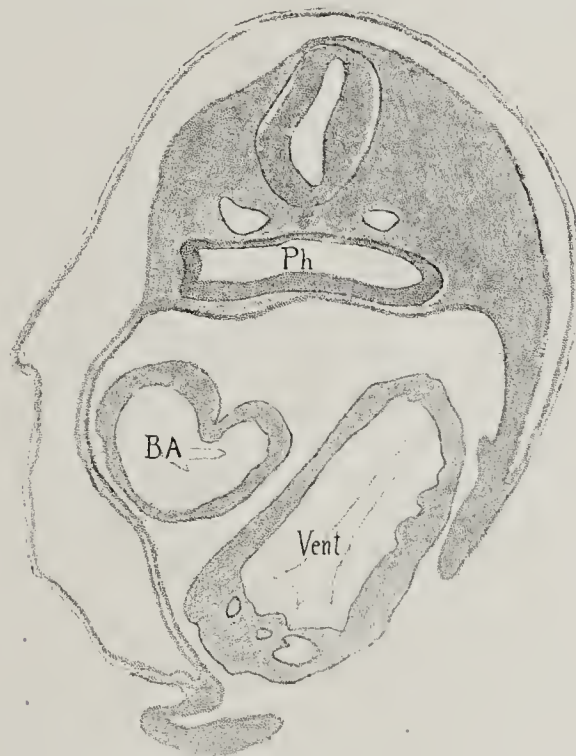


FIG. 6.—Section through the head of the embryo 3.5 mm. long. No. CLXIV $\times 50$ times; *ph*, pharynx; *ba*, bulbous aortae; *vent*, ventricle.

ovum was hardened in 80 per cent alcohol shortly after it was expelled from the uterus. This of course fixed the embryo in its natural shape, as was the case with No. XII. Both embryos are curved, but in the embryo 4.3 mm. long the branchial region occupies relatively more space than it

³ A photograph of this embryo is given in the Weleh Festschrift.

does in the embryo 2.1 mm. long. In proportion to the length of the embryos this distance has increased 3 times. The pericardial coelom has receded from the head in proportion to the increase of the growth of the branchial arches. In the embryo 2.1 mm. long the head end of the pericardial coelom is opposite the otic vesicle, while in the embryo 4.3

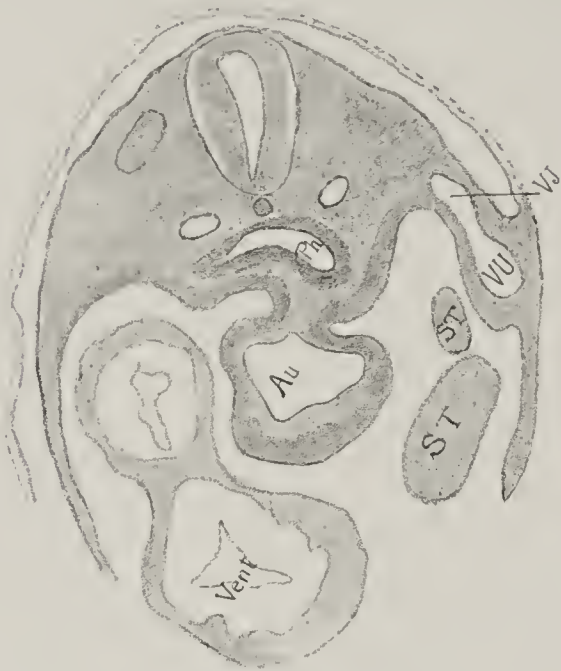


FIG. 7.—Section through the embryo 3.5 mm. long, .14 mm. nearer the tail than Fig. 6 $\times 50$ times; *ph*, pharynx; *au*, auricle; *vent*, ventricle; *st*, septum transversum; *vj*, jugular vein; *vu*, umbilical vein.

mm. it is opposite the first occipital myotome. The point of communication between the peritoneal coelom (encircling the liver) with the exocoelom has also receded. In the embryo 2.1 mm. long it is opposite the second cervical myotome; in embryo 4.3 mm. long opposite the second thoracic myotome



FIG. 8.—Section through the embryo 3.5 mm. long, .2 mm. nearer the tail than Fig. 7 $\times 50$ times; *l*, liver; *vent*, ventricle; *sr*, sinus reniens; *coe*, coelom.

(compare Figs. 1 and 10). His's embryo *Lr* (4.2 mm. long) is intermediate between the two embryos just compared. In *Lr* (see His's Atlas, Pls. IX and XI) the pericardial, pleural and peritoneal coelom encircling the liver extends from the first occipital myotome to the sixth cervical, and the omphalo-mesenteric veins protrude into these canals of the coelom. The liver has extended into the septum transversum but does not yet encircle the omphalo-mesenteric veins as it does in

my embryo 4.3 mm. long. This detailed description is given to show the fate of the coelom⁴ of the head and neck. It gives rise to the pericardial and pleural cavities, and that portion of the peritoneal cavity encircling the liver of the adult.

Sections of the embryo 4.3 mm. long (No. CXLVIII, Figs. 11 and 12) show the liver sprouts growing in all direc-

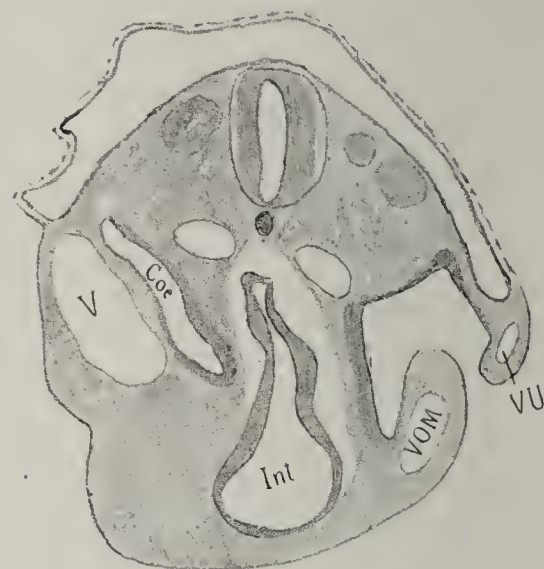


FIG. 9.—Section through the embryo 3.5 mm. long, .18 mm. nearer the tail than Fig. 8 $\times 50$ times; *coe*, coelom; *int*, intestine; *vom*, omphalo-mesenteric vein; *vu*, umbilical vein.

tions through the septum transversum, encircling and ramifying through the omphalo-mesenteric veins, making a condition slightly in advance of that in His's embryo *Lr*. The sections of this embryo show clearly that the heart, lungs, liver and lower peritoneal cavity arise in tissues surrounded by that portion of the coelom extending into the head in Embryo XII.

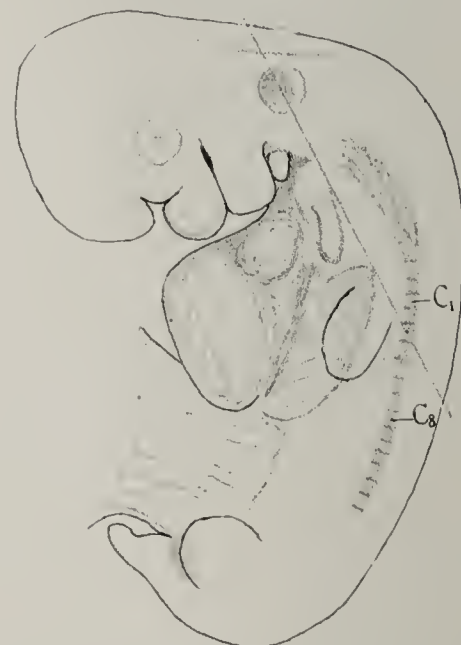


FIG. 10.—Outline of the embryo 4.3 mm. long. No. CXLVIII $\times 15$ times. *C*₁, first cervical myotome; *C*₈, eighth cervical myotome. The line indicates the direction of the sections.

Fig. 1. Fig. 11 is taken from a section through a plane cutting the root of the arm and the otic vesicle, and can readily be placed in the outline, Fig. 10. It is seen that the lungs arise where the pericardial coelom goes over into the pleural, *i. e.* high up in the region of the head. Immediately on the dorsal side of them is the beginning of the lesser peritoneal

⁴ Kopfhöhle; Halshöhle; Parietalhöhle and recessus parietalis.

cavity, and the intestinal tube struck in this section is the stomach. All these structures lie on the cephalic side of the first cervical myotome. Projecting into the peritoneal coelom, encircling and penetrating the omphalo-mesenteric veins are the projections of the liver, Figs. 11 and 12, *L*. The two lobes reach from the tip of the lungs and the foramen of Winslow to the point where the entodermal cells of the liver arise from

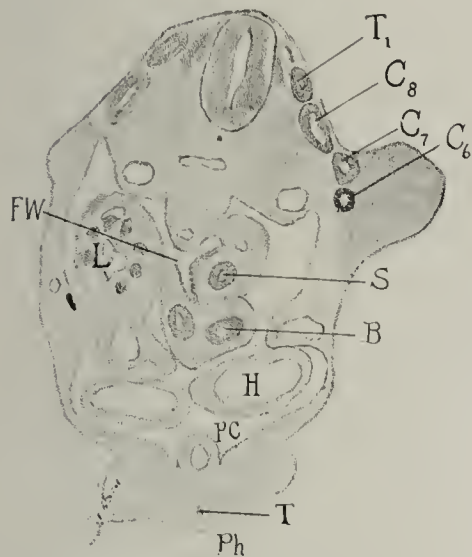


FIG. 11.—Section through the embryo 4.3 mm. long \times 25 times; *T*₁, first thoracic myotome; *C*, *C*₇, and *C*₈, cervical myotomes; *s*, stomach; *fb*, bronchus; *h*, heart; *t*, thyroid; *pc*, pericardial cavity; *l*, liver; *fw*, foramen of Winslow.

the alimentary canal, or in this case the duodenum. The lobes of the liver lie entirely within the canals of the coelom on either side of the head. The caudal ends of these coelom canals have migrated from opposite the second cervical myotome in Embryo XII, Fig. 1, to opposite the second thoracic

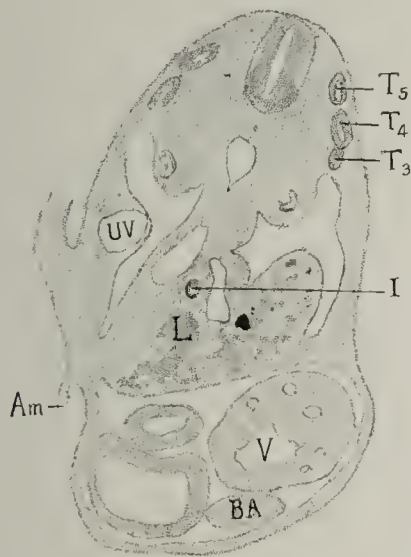


FIG. 12.—Section through the embryo 4.3 mm. long, .4 mm. deeper than Fig. 11 \times 25 times; *T*, thoracic myotomes; *i*, intestine; *l*, liver; *v*, ventricle; *ba*, bulb of the aorta; *am*, amnion; *uv*, umbilical vein.

myotome in Embryo CXLVIII, Fig. 10. It has moved towards the tail eight segments, while the cephalic end of the canal, the pericardial coelom, has been kinked over to correspond with the bending of the head, has dilated to correspond with the growth of the heart, and has receded from the otic vesicle to the extent of the growth of the branchial arches. We have in this embryo the necessary stage to locate the organs which arise in the neighborhood of the septum trans-

versum, as well as to give the fate of the coelom in their immediate neighborhood.

A stage somewhat in advance of CXLVIII is LXXVI. The embryo is slightly larger, measuring 4.5 mm. in greatest length. It was obtained from the uterus 7 hours after death. The entire ovum was placed immediately in absolute alcohol.

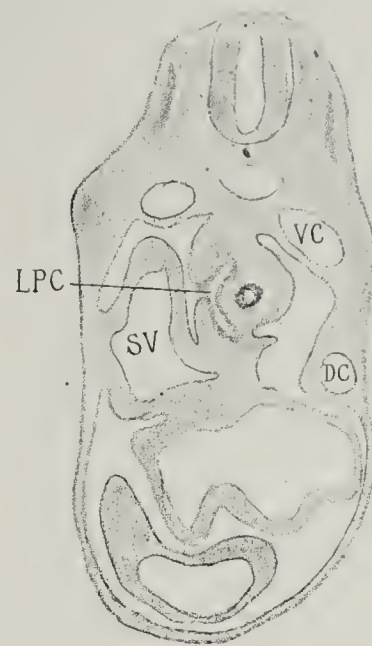


FIG. 13.—Section through the embryo 4.5 mm. long. No. LXXVI \times 25 times; *vc*, cardinal vein; *lpc*, lesser peritoneal cavity; *dc*, ductus Cuvieri; *sv*, sinus venosus.

It was impossible to obtain a picture of the embryo before it was cut, but the specimen proved to be an excellent one. The direction of the sections is more nearly transverse than

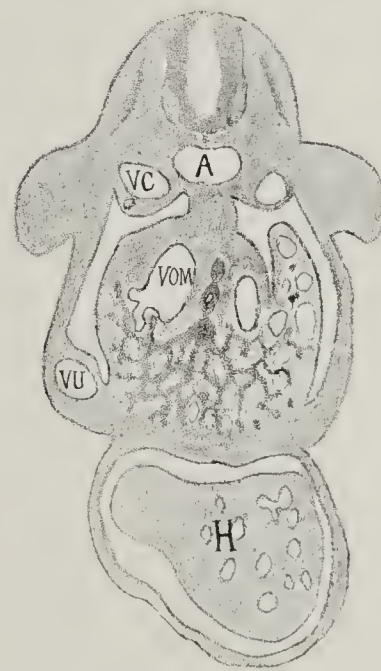


FIG. 14.—Section through the embryo 4.5 mm. long, .6 mm. deeper than Fig. 13 \times 25 times; *vc*, cardinal vein; *a*, aorta; *vom*, omphalo-mesenteric vein; *uv*, umbilical vein; *h*, heart.

in CXLVIII. In CXLVIII the neuropore is closed with a thickening of the epidermis just over the point of closure; the umbilical vein enters the liver and its direct connection with the ductus Cuvieri through the body wall is cut off. In LXXVI the neuropore is completely closed and the embryo is somewhat larger than before (compare Figs. 13 and 11 with 11 and 12); the umbilical vein, however, communicates with the ductus Cuvieri through the body-wall on the left

side. This is an instance of retarded development of a part, as the left umbilical vein should have vanished by this time.

Fig. 13 gives a section through the foramen of Winslow immediately on the caudal side of the lung buds, as shown in a lateral view of the model of the embryo, Fig. 15. The

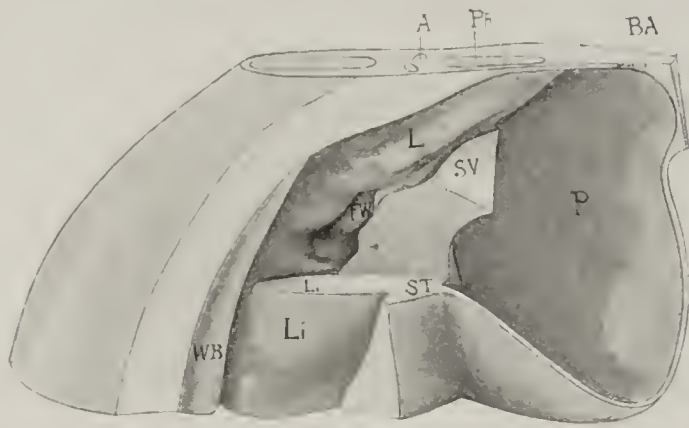


FIG. 15.

septum transversum and liver have increased in quantity, as a comparison of the different figures will show. In this

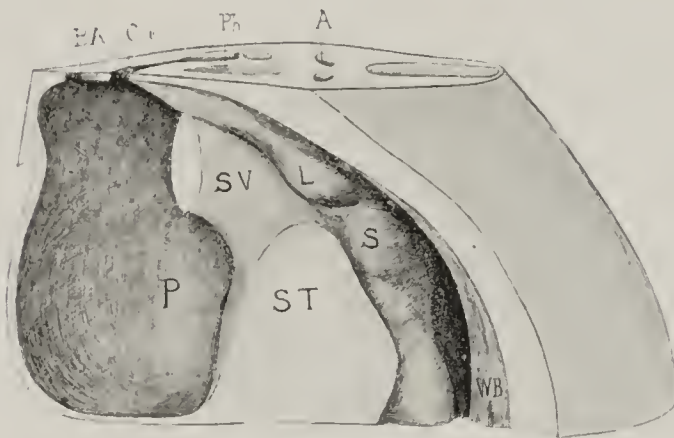


FIG. 16.

FIGS. 15 and 16.—Right and left views of a reconstruction of the embryo 4.5 mm. long $\times 25$ times; *a*, aorta; *ph*, pharynx; *ba*, bulbus aortae; *cac*, coelom; *p*, pericardial coelom; *l*, lung; *li*, liver; *wb*, Wolffian body; *s*, stomach; *fw*, foramen of Winslow; *sv*, sinus venosus; *st*, septum transversum.

stage we have the extreme bending of the head, which throws the heart to its most ventral point with the septum transversum about parallel with long axis of the embryo. The

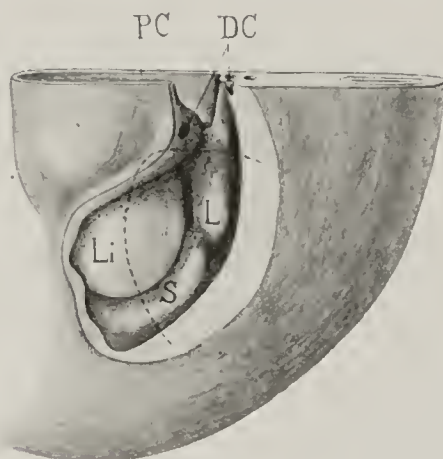


FIG. 17.—Lateral view of the reconstruction of an embryo 5 mm. long. No. LXXX $\times 17$ times; *l*, lung; *li*, liver; *s*, stomach; *dc*, ductus Cuvieri; *pc*, pericardial coelom which communicates fully with pleuro-peritoneal coelom.

position of the heart, lungs, liver and their relation to the coelom is much the same as in the younger embryo with the

exception of the lesser peritoneal cavity, which is now more to the caudal side of the lungs.

While in the embryo 4.3 mm. long the myotomes were well formed and hollow, in the embryo 4.5 they are solid and contain embryonic muscle fibres. The dorsal ganglia are also

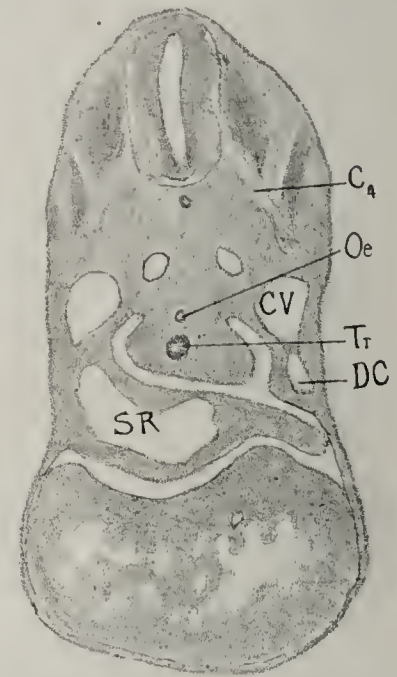


FIG. 18.—Section through the neck and heart of embryo LXXX $\times 25$ times; *C₄*, fourth cervical nerve; *oe*, oesophagus; *cv*, cardinal vein; *dc*, ductus Cuvieri; *tr*, trachea; *sr*, sinus rennens.

more developed. In the embryos 5 mm. long (LXXX and CXXXVI) the myotomes are still further differentiated with nerve trunks, composed of both dorsal and ventral roots, which are growing into the body-walls of the embryo. Figs. 17-20 give the general form of this embryo, in reconstruction

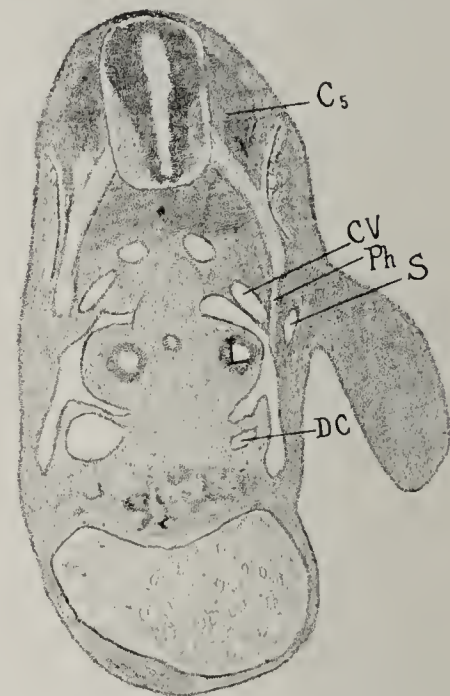


FIG. 19.—Section through embryo LXXX .22 mm. deeper than Fig. 18 $\times 25$ times; *C₅*, fifth cervical nerve; *cv*, cardinal vein; *s*, subclavian vein; *dc*, ductus Cuvieri; *l*, lung; *ph*, phrenic nerve.

as well as in section. The septum transversum is not as perpendicular as in either younger or older stages (LXXVI and II), but in general this embryo is intermediate between them. A separation between the pericardial and pleural coelom now begins to make its appearance by means of a constriction in its walls, the ductus Cuvieri encircling the coelom at this point. The lung buds hang free into the pleural coelom,

and the liver and stomach into the peritoneal coelom. The ductus Cuvieri lies in a ridge of tissue encircling the canal of communication between the pericardial and pleural coelom. In this embryo the ridge has no mesentery, as described by His (Fig. 18), but in sagittal sections of the same stage (CXXXVI) the mesentery is present. As yet there is no

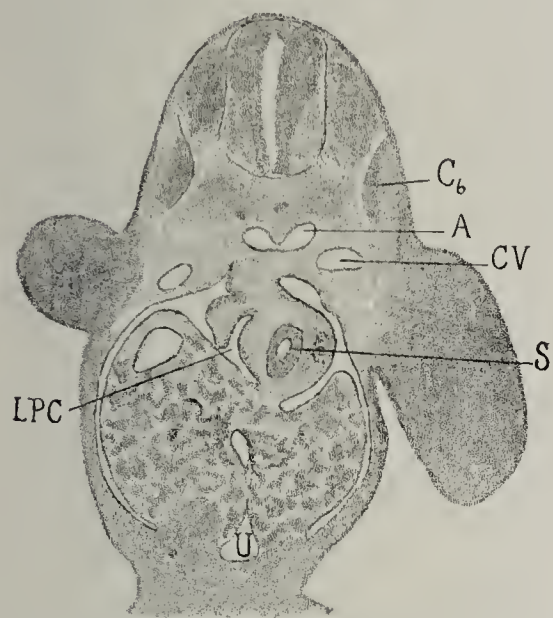


FIG. 20.—Section through embryo LXXX, .26 mm. deeper than Fig. 19 \times 25 times; *C*₆, sixth cervical myotome; *a*, aorta; *cv*, cardinal vein; *s*, stomach; *u*, umbilical vein; *lpc*, lower peritoneal cavity.

indication of a line of separation between the pleural and peritoneal coelom in LXXX, but in CXXXVI there is an elevation on the dorsal wall of the pleural coelom, Fig. 21, which encircles the lung and joins the dorsal end of the septum transversum. This is one of the pillars of Uskow

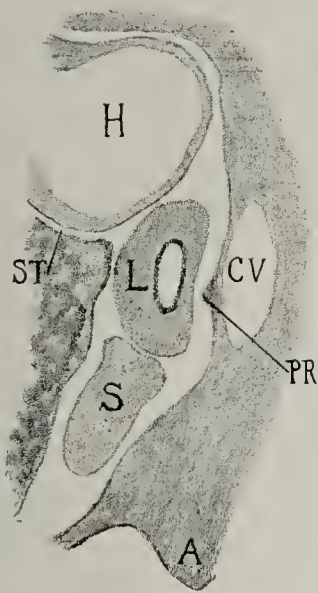


FIG. 21.—Sagittal section through an embryo, 5 mm. long. No. CXXXVI \times 25 times; *h*, heart; *cv*, cardinal vein; *st*, septum transversum; *l*, lung; *s*, stomach; *a*, arm; *pr*, pulmonary ridge.

or the beginning of a ridge which I shall term the *pulmonary ridge*.

Fig. 20, compared with Fig. 13, shows that the foramen of Winslow has moved more rapidly towards the tail than the heart. A section through it strikes the heart squarely in one case, while in the other it does not touch the heart but strikes the liver only. This is in part due to the direction of the section in the two specimens, and in part to the shifting of the foramen of Winslow with the recession of the

stomach. The cervical nerves are separated in No. LXXX with the exception of an anastomosis between the fourth and the fifth. From this point the phrenic nerve arises, Fig. 19, and passes to the lateral side of the parietal coelom and lung. In a later stage it reaches the septum transversum through the pleuro-pericardial membrane of Uskow.

I have now followed the transformation of the relatively simple coelom of the head and neck from the time it is well formed in an embryo of the end of the second week to the end of the third week. During this time the pericardial coelom has moved away from the head and the pericardial cavity is well outlined, but the membranes which divide the coelom into pericardial, pleural and peritoneal spaces have not yet

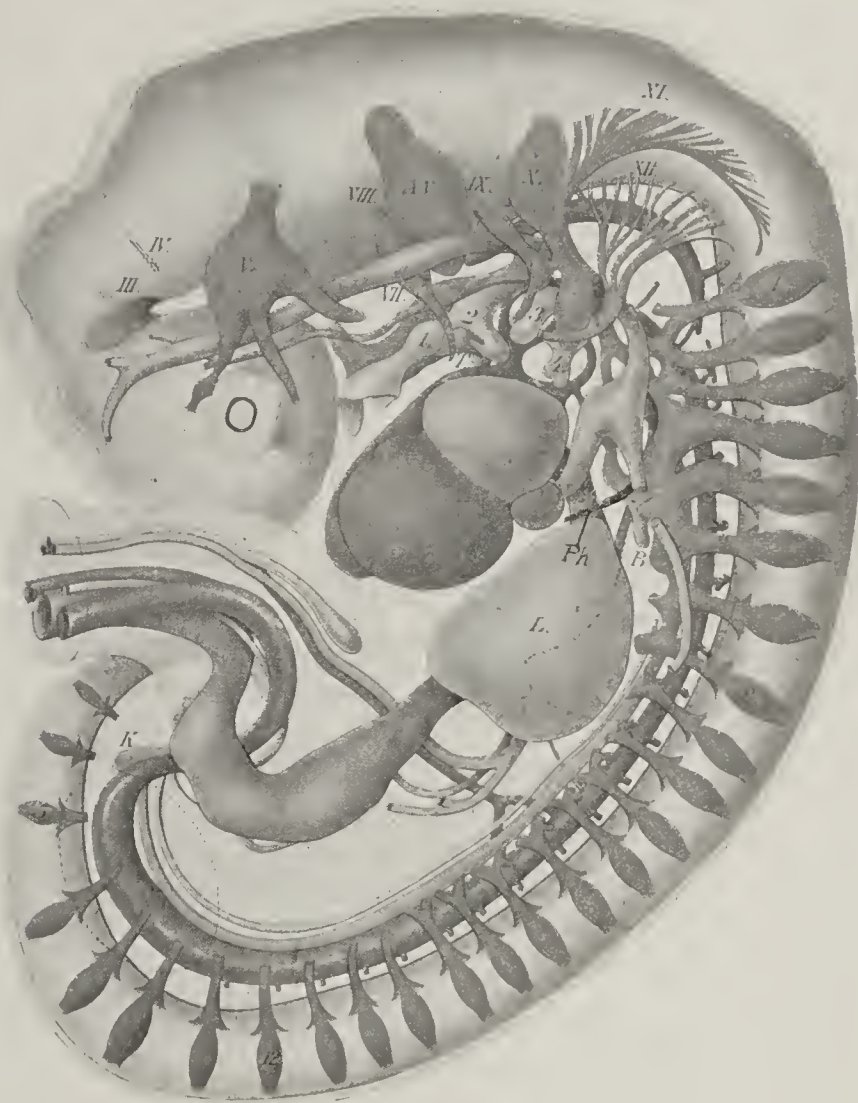


FIG. 22.—Reconstruction of embryo No. II \times 20 times; *B*, bronchus; *L*, liver; *Ph*, phrenic; 1, 2, 3, 4 branchial pouches.

appeared. During the fourth week both of these membranes appear, but they are not well defined until the fifth week.

Fig. 22 is from a profile reconstruction of Embryo II, showing the relation of the organs to one another. A east of the colon of this embryo is given in Fig. 23. The extreme ventral kinking of the heart is shown in this stage and from now on it begins to sink more and more into the body as the liver recedes. The communication between the pericardial coelom and the pleural coelom is reduced to a narrow slit between the cephalic end of the lung bud and the ductus Cuvieri. It appears as if a simple adhesion of the walls of the slit would complete the closure of the pericardial space. Fig. 24 is a section through this space, striking the seventh cervical myo-

tome and the tip of the phrenic nerve. It shows that the attachment of the ductus Cuvieri is no longer broad, as in embryo LXXX, but is narrow, forming a mesentery as de-



FIG. 23.—Cast of coelom of embryo 11 \times 20 times; *P*, pericardial coelom; *L*, coelom encircling to liver.

scribed by His. On the dorsal side of the ductus there is a ridge which begins as the ductus projects into the coelom and gradually runs over into the lobe of the liver. This ridge is very pronounced and is also well shown in the sections of

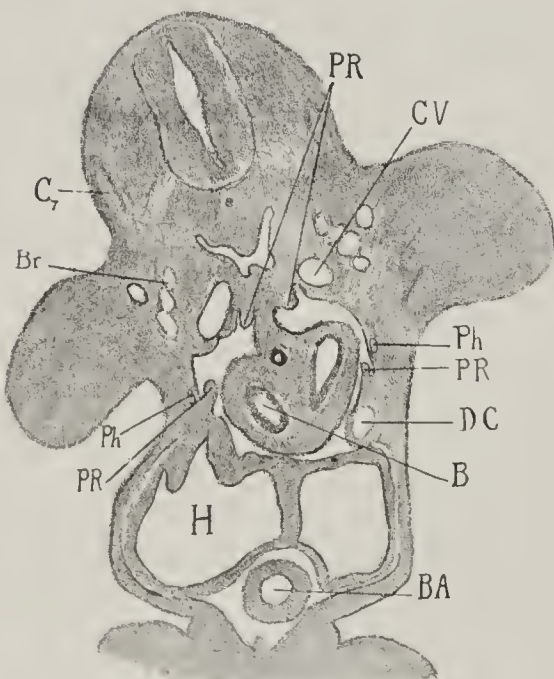


FIG. 24.—Section through the seventh cervical segment of the embryo 7 mm. long. No. 11 \times 25 times; *C*₇, seventh cervical myotome; *cv*, cardinal vein; *dc*, ductus Cuvieri; *br*, brachial plexus; *pr*, pulmonary ridge; *ph*, phrenic nerve; *b*, bronchus; *h*, heart; *ba*, bulbus aortae.

His's embryos, A and B, as given in his *Atlas*. The relation of this ridge to the phrenic nerve as well as its form in older embryos makes of it the *Anlage* of both the pleuro-pericardial and pleuro-peritoneal membranes. It lies in the sagittal plane

of the coelom and as it passes the region of the fourth and fifth cervical nerves receives into its substance the phrenic nerve which passes on the caudal side of the ductus Cuvieri. Soon the lung bud grows against this ridge, causes it to bulge, and with the rotation of the liver towards the head the ridge

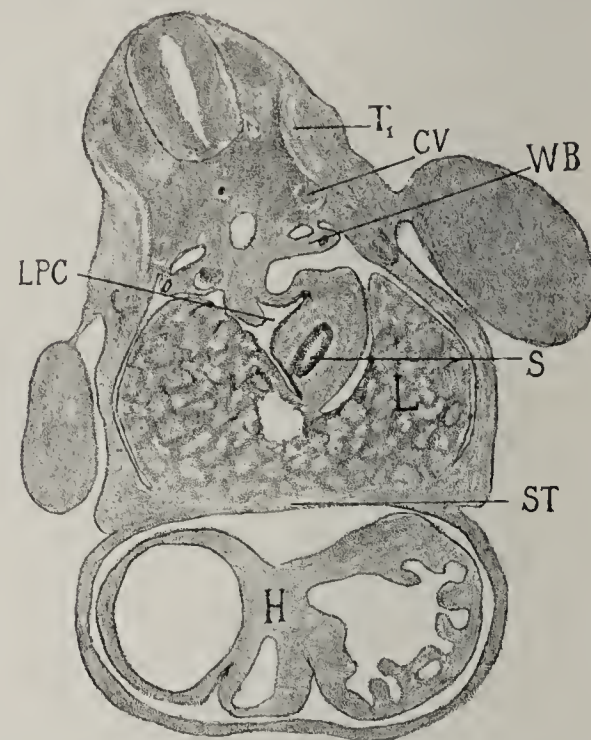


FIG. 25.—Section through the embryo 7 mm. long, .6 mm. deeper than Fig. 24 \times 25 times; *T*₁, first thoracic myotome; *cv*, cardinal vein; *wb*, Wolffian body; *s*, stomach; *lpc*, lesser peritoneal cavity; *l*, liver; *h*, heart; *st*, septum transversum.

is divided into two parts; (1) the cephalic end which retains the phrenic nerve and ductus Cuvieri and forms the pleuro-pericardial membrane, and (2) the caudal end which remains attached to the tip of the dorsal end of the septum trans-

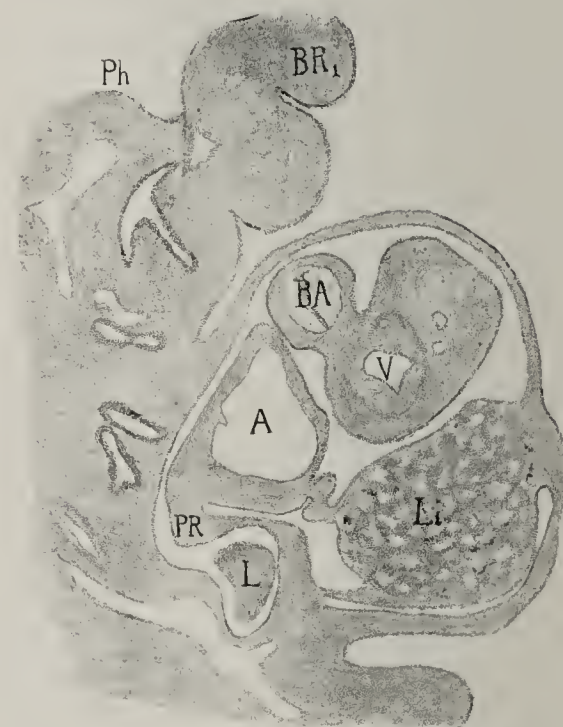


FIG. 26.—Sagittal section through the embryo 6.5 mm. long. No. CXVI \times 25 times; *ph*, pharynx; *br*₁, first branchial arch; *ba*, bulbus aortae; *a*, auricle; *v*, ventricle; *l*, lung; *li*, liver; *pr*, pulmonary ridge.

versum and the liver on the one hand, the body-wall on the other, to form the pleuro-peritoneal membrane.

Figs. 26-28 show this ridge in sagittal sections in Embryo CXVI, a specimen not quite as large as No. 11, but somewhat

more advanced in development. In Fig. 26 its cephalic end appears as a broad membrane which in a section nearer the middle line extends to the liver on the ventral side and

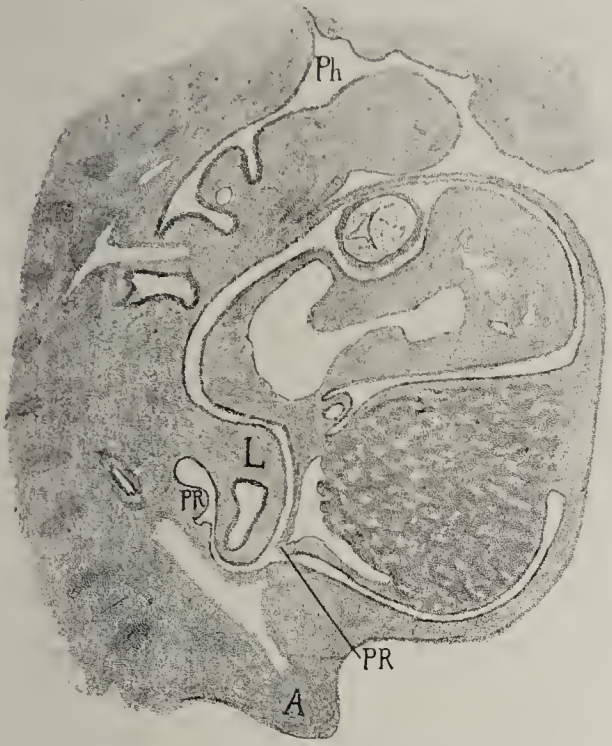


FIG. 27.—Section through the embryo 6.5 mm. long, .1 mm. deeper than Fig. 26 $\times 25$ times, *ph*, pharynx; *a*, arm; *pr*, pulmonary ridge; *l*, lung.

it begins to widen at its dorsal end hand in hand with the rotation of the liver. Up to this time the septum transversum is parallel with the vertebral column, with the heart

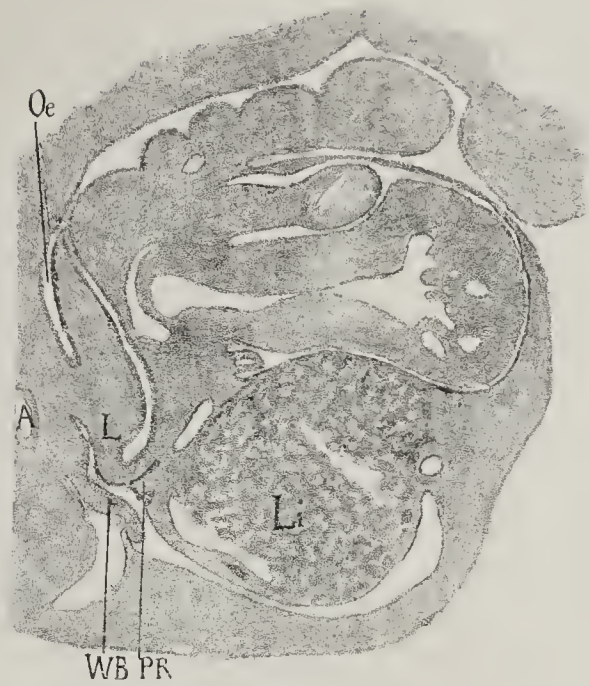


FIG. 28.—Section through the embryo 6.5 mm. long, .12 mm. deeper than Fig. 27 $\times 25$ times; *oe*, oesophagus; *a*, aorta; *l*, lung; *li*, liver; *Wb*, Wolffian body; *pr*, pulmonary ridge.



FIG. 29.—Lateral view of the pulmonary membrane and surrounding parts of the embryo 7 mm. long. No. II $\times 30$ times; *a*, auricle; *v*, ventricle; *l*, lung; *li*, liver; *Wb*, Wolffian body; *pr*, pulmonary ridge; *C₈*, eighth cervical myotome.

accompanies the ductus Cuvieri to the body-wall on the dorsal side, Fig. 27, *pr*. Still more towards the midline the ridge ends as a decided elevation immediately to the caudal side of the tip of the lung.

After the pulmonary ridge is well formed (as in Embryo II)

on its ventral side and the liver on its dorsal side projecting into the peritoneal coelom, as shown in No. II. This condition was brought about at the time of the bending of the head when the viscera were forced towards the tail and into this position. The cephalic end of the pericardial coelom

is thus bent over the septum transversum but the main part of the head coelom remained parallel with the spinal column on either side of the body. This process may be termed the rolling over of the heart.

In the next stage the heart rolls in a dorsal direction and the liver in a ventral direction. This process has already begun in embryo CLXIII and CLXIII. In so doing the lung buds become buried deeper in the body of the embryo and the liver gradually changes its position from the dorsal side

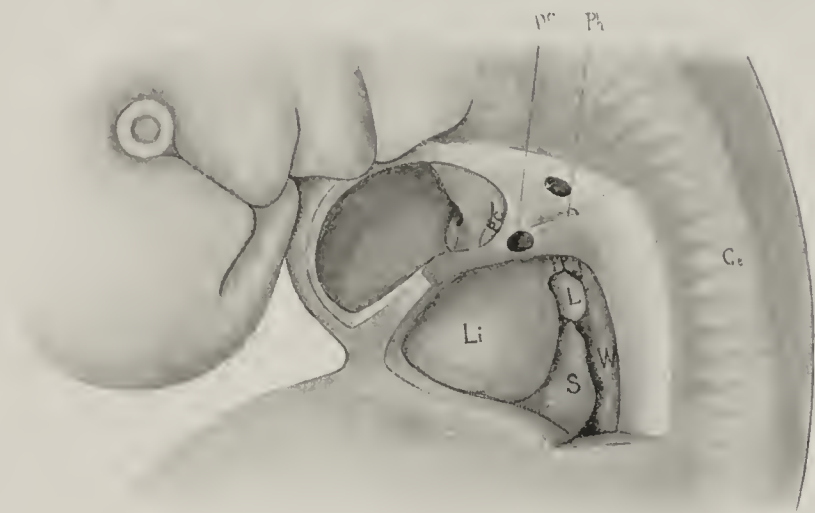


FIG. 30.—Lateral view of the pulmonary membrane and surrounding parts of the embryo 9 mm. long; No. CLXIII $\times 12\frac{1}{2}$ times; C_8 , eighth cervical myotome; Li , liver; L , lung; S , stomach; Wb , Wolffian body; ph , phrenic nerve; pc , pleuro-pericardial membrane; pp , pleuro-peritoneal membrane.

of the septum transversum to its ventral side. The septum transversum undergoes almost a half-revolution. The coelom containing the liver lobe evaginates and becomes incorporated with the general abdominal cavity.

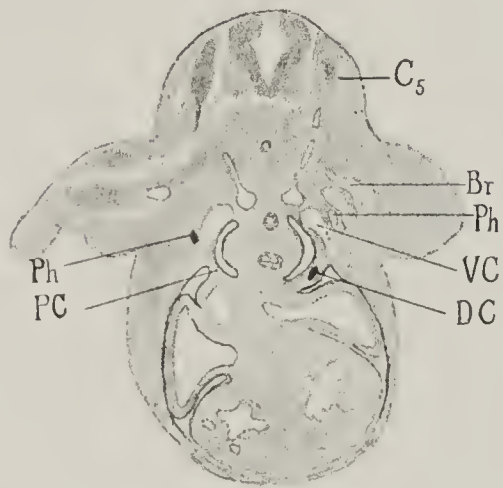


FIG. 31.—Section through the fifth cervical myotome of the embryo 9 mm. long, No. CLXIII $\times 12\frac{1}{2}$ times; C_5 , fifth myotome; vc , cardinal vein; dc , ductus enveri; br , brachial plexus; ph , phrenic nerve; pc , cephalic end of the pulmonary ridge forming the beginning of the pleuro-pericardial membrane.

With the rolling of the heart the coelom connecting the pericardial with the pleural space is kinked at the points of juncture between these cavities. At this point the duct of Cuvier enters the heart. Soon from its dorsal border the pulmonary ridge arises which is semicircular in form and reaches from the liver to the dorsal walls of the coelom as described under Embryo II. It is shown in section in Fig. 24, and in a lateral reconstruction in Fig. 29. The pulmon-

ary ridge is really an extension of the septum transversum from the lobes of the liver to the tip of the Wolffian body. As the heart moves in the dorsal direction and the liver in the ventral direction it is the dorsal end of the septum trans-

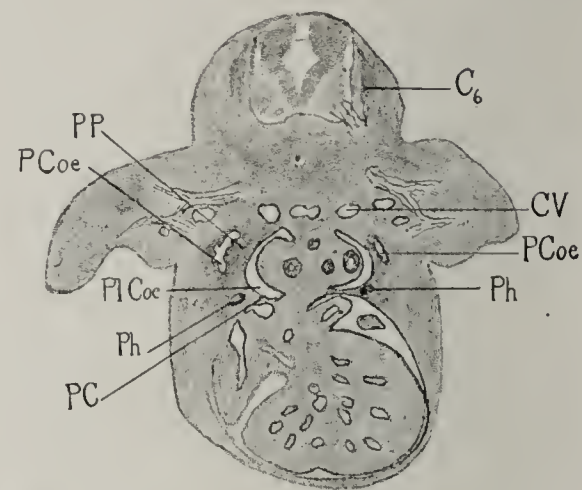


FIG. 32.—Section through the embryo 9 mm. long, .16 mm. deeper than Fig. 31 $\times 12\frac{1}{2}$ times; C_6 , sixth cervical myotome; cv , cardinal vein; ph , phrenic nerve; pc , pleuro-pericardial membrane; pp , pleuro-peritoneal membrane; $pl-coe$, pleural coelom; $p-coe$, peritoneal coelom.

versum which moves most rapidly in the direction of the tail. In so doing the pulmonary ridge grows rapidly and divides at its dorsal end into two membranes, one containing the

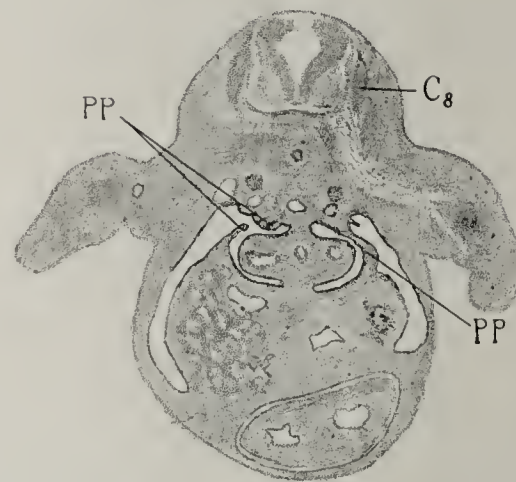


FIG. 33.—Section through the embryo 9 mm. long, .16 mm. deeper than Fig. 32 $\times 12\frac{1}{2}$ times; C_8 , eighth cervical nerve; pp , pleuro-peritoneal membrane.

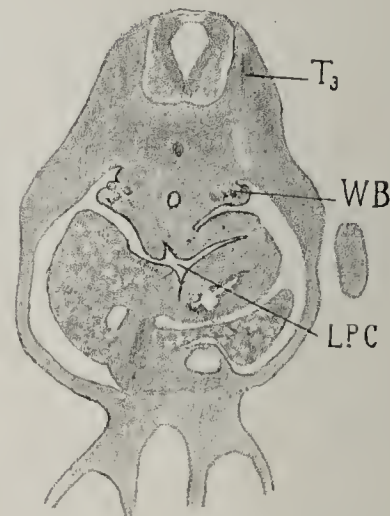


FIG. 34.—Section through the embryo 9 mm. long, .84 mm. deeper than Fig. 33 $\times 12\frac{1}{2}$ times; T_3 , third thoracic myotome; lpc , lower peritoneal cavity; Wb , Wolffian body.

duct of Cuvier and phrenic nerve, and the other still encircling the lung bud. In this division we have the beginnings of the pleuro-pericardial membrane of Uskow, and the pleuro-peritoneal membrane of Brachet.

The pulmonary ridge is well formed in Embryo II. It appears as a ridge of tissue passing towards the head from the lobe of the liver on the dorsal side of the ductus Cuvieri and then along the dorsal walls of the coelom to the meso-

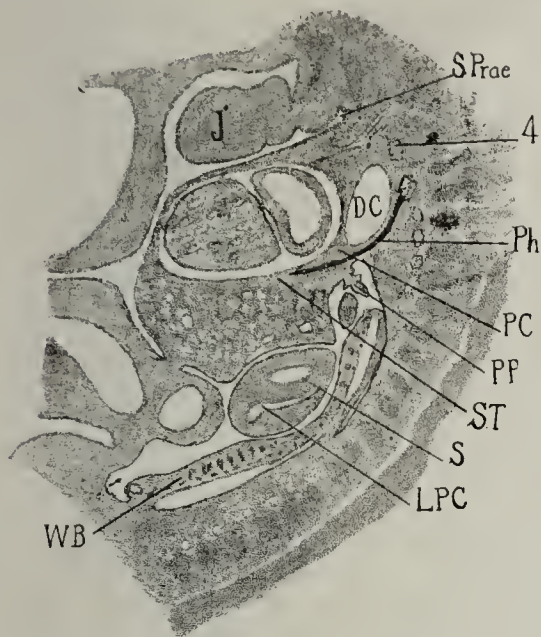


FIG. 35.—Sagittal section through the embryo 8 mm. long, No. CXIII $\times 10$ times; *j*, lower jaw; *s-prae*, sinus praeecervicalis; *4*, fourth cervical nerve; *ph*, phrenic nerve; *st*, septum transversum; *dc*, ductus Cuvieri; *pc*, pleuro-pericardial membrane; *pp*, pleuro-peritoneal membrane; *l*, lung; *s*, stomach; *lpc*, lower peritoneal cavity; *Wb*, Wolffian body.

cardium, where it ends in the pillars of Uskow. As the embryo grows larger the ductus Cuvieri separates more and more from the lateral body-wall, and in a measure shifts into the pulmonary ridge, which at its most convex point grows in the form of a ridge towards the heart. This secondary ridge, which is present in CLXIII, finally separates the pleural from the pericardial cavities and completes the pleuro-pericardial membrane.

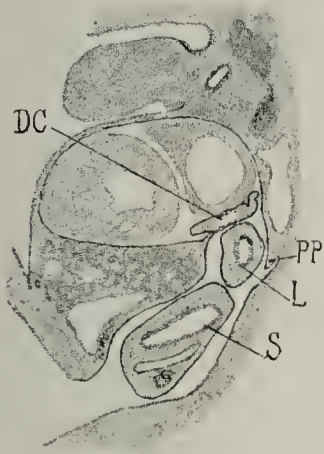


FIG. 36.—Section through the embryo 8 mm. long nearer the middle line than Fig. 35 $\times 10$ times; *dc*, ductus Cuvieri; *l*, lung; *s*, stomach; *pp*, pleuro-peritoneal membrane.

The pulmonary ridges from their beginning to their separation into the pleuro-pericardial and pleuro-peritoneal membranes appear as two ears to the septum transversum, extending along the ducts of Cuvier in the sagittal plane of the body and at right angles to the plane of the septum transversum. Judging by the relation of the phrenic nerve to the pulmonary ridge the portion of it on the dorsal side of the ductus Cuvieri containing the phrenic nerve, the portion containing the ductus Cuvieri, and the secondary ridge of the

ventral side of the ductus Cuvieri, form the pleuro-pericardial membrane. The portion of the pulmonary ridge on the caudal side of the phrenic nerve gives rise to the pleuro-peritoneal membrane. In so doing it gradually shifts over



FIG. 37.—Sagittal section through the embryo 10 mm. long, No. CXIV $\times 10$ times; *pp*, pleuro-peritoneal membrane.

the lung buds and finally completely separates the pleural from the peritoneal cavities.

The growth of the pleuro-pericardial membrane towards

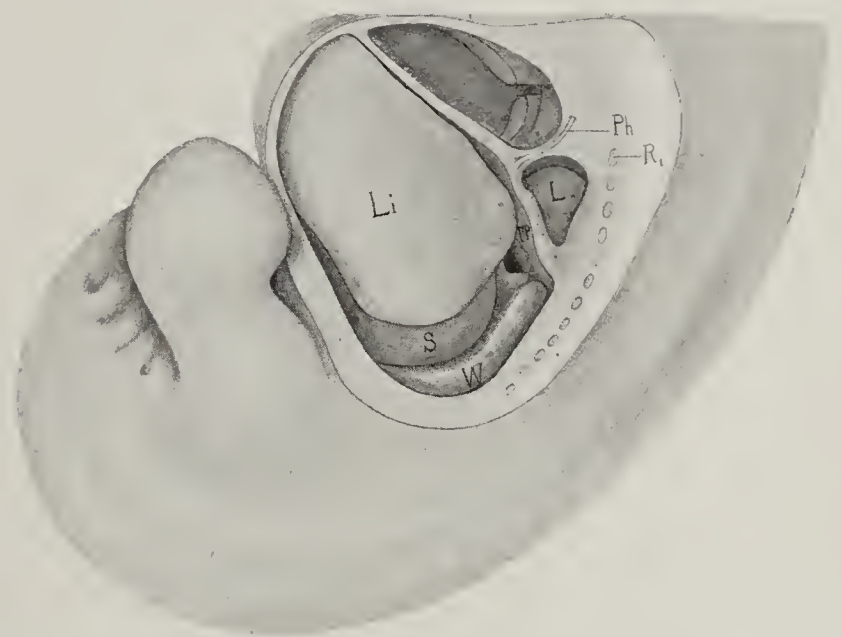


FIG. 38.—Lateral view of the embryo 11 mm. long, showing the pleuro-pericardial and pleuro-peritoneal membranes. No. CIX $\times 8\frac{1}{2}$ times; *r1*, first rib; *l*, lung; *li*, liver; *ph*, phrenic nerve in the pleuro-pericardial membrane; *s*, stomach; *Wb*, Wolffian body; *pp*, pleuro-peritoneal membrane which is not quite completed.

the head and the pleuro-peritoneal towards the tail widens the dorsal projection of the septum transversum and into this wide base the lung burrows throwing the pleuro-pericardial membrane with the phrenic nerve to its medial side.

The fate of the pulmonary ridge is shown in Fig. 30, which is from Embryo CLXIII. Sections of this embryo are shown in Figs. 31 to 34. They show again that the pulmonary ridge reaches from the ductus Cuvieri to the tip of the lung, and the phrenic nerve. It is readily seen from Figs. 30 and

32 how the phrenic nerve is pushed to its permanent position by the further rotation and recession of the septum transversum and liver, and the lateral growth of the lungs to encircle the heart.

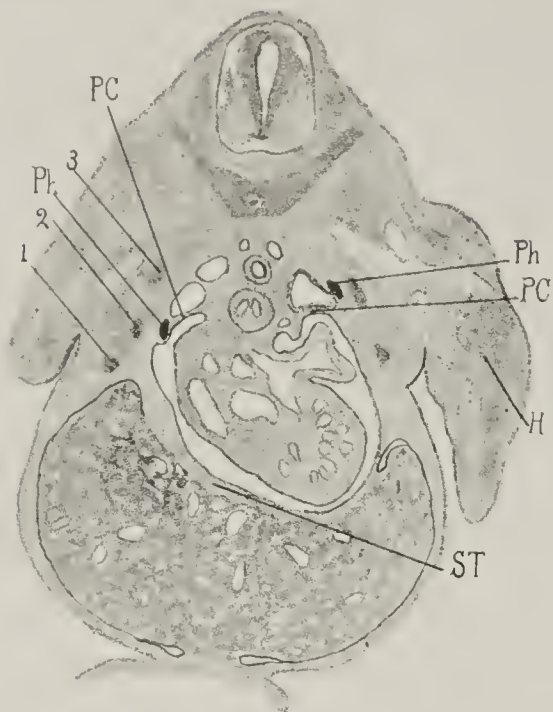


FIG. 39.—Section through the body of the embryo 11 mm. long. No. CLX $\times 10$ times; *ph*, phrenic nerve; *pc*, pleuro-pericardial membrane; *st*, septum transversum; *h*, humerus; *3*, first rib; *2*, second rib; *1*, third rib.

Figs. 35 and 36 are from sagittal sections of Embryo CXIII, which is of the same stage as CLXIII. The phrenic nerve is shown throughout its whole course from the fifth cervical nerve to the pleuro-pericardial membrane. The nerve receives a second branch a few sections deeper from the sixth cervical which unites with the main trunk before it enters

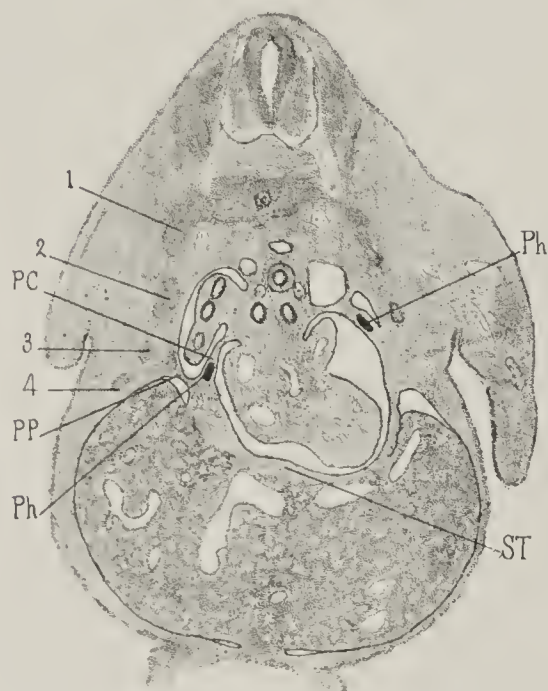


FIG. 40.—Section through the embryo 11 mm. long; .18 mm. deeper than Fig. 39 $\times 10$ times; *ph*, phrenic nerve; *st*, septum transversum; *pc*, pleuro-pericardial membrane; *pp*, pleuro-peritoneal membrane; *1*, *2*, *3*, *4*, ribs.

the pleuro-pericardial membrane. Hanging from the pleuro-pericardial membrane is a section of the pleuro-peritoneal, which in Fig. 36 unites with the dorsal wall of the coelom at the head end of the Wolffian body.

About this time the portion of the pulmonary ridge des-

tined to become the pleuro-pericardial membrane unites with the root of the lung bud and completely closes the pericardial cavity, Fig. 37. By this union the course of the ductus Cuvieri is from the body-wall to the heart through the pleuro-pericardial membrane, and the plane of the pleuro-pericardial



FIG. 41.—Section through the embryo 11 mm. long, .46 mm. deeper than Fig. 40 $\times 10$ times. The pleuro-peritoneal membrane is incomplete on one side, *3*, *4*, *5*, *6*, ribs.

membrane is practically that of the septum transversum, the two together being transverse to the body of the embryo. The phrenic nerve at this time is in the plane of the septum transversum and reaches its dorsal tip through its projection, the pleuro-pericardial membrane.

Immediately after the completion of the pleuro-pericardial

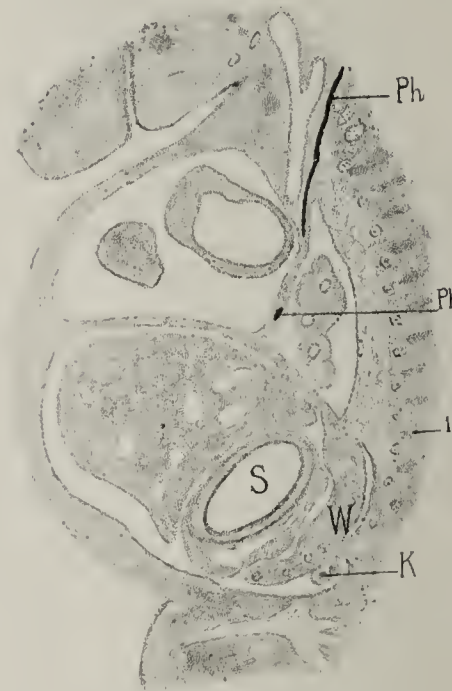


FIG. 42.—Sagittal section through the embryo 14 mm. long. No. CXLIV $\times 10$ times, *ph*, phrenic nerve; *10*, tenth rib; *s*, stomach; *k*, kidney; *W*, Wolffian body.

membrane the rotation of the liver and septum transversum is accelerated, and by the time the embryo has grown to be 11 mm. long (CIX), the liver is practically in its adult position. The rapid rotation of the liver, especially at its dorsal end, has changed the relation of the planes between the

pleuro-pericardial membrane to the septum transversum from parallel to right angles. Now the septum transversum is in the plane of the pleuro-peritoneal membrane (Fig. 38). With the recession of the septum transversum, especially at its

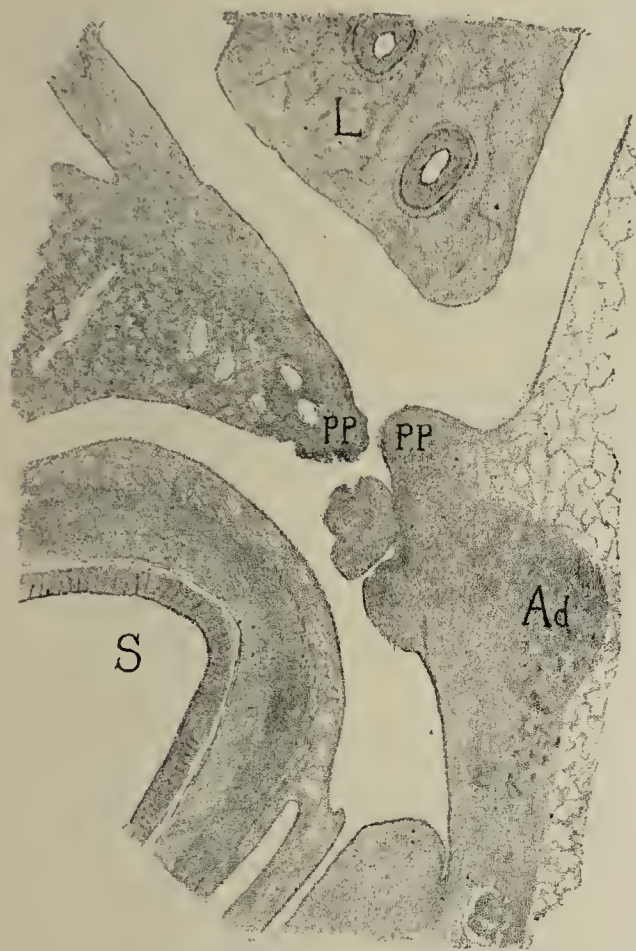


FIG. 43.—Section through the opening between the pleural and peritoneal cavities in the embryo 14 mm. long \times 50 times; *s*, stomach; *l*, lung; *pp*, pleuro-peritoneal membrane; *ad*, adrenal.

dorsal end, the evagination of the coelom containing the liver and stomach is complete, throwing them into the general peritoneal cavity.

Figs. 39, 40 and 41 are sections through the pleuro-peri-



FIG. 44.—Sagittal section through the body of the embryo 16 mm. long. No. XLIII \times 10 times; 9, ninth rib.

cardial and pleuro-peritoneal membranes of Embryo CIX, Fig. 38. They give the relation of the pleuro-pericardial and pleuro-peritoneal membranes to the surrounding structures. The heart is now in its permanent location in the thorax and

the liver is in the abdominal cavity. The septum transversum with its extension, the pleuro-peritoneal membrane, stretches across the body from the tips of the embryonic ribs. But in the thorax lie the lungs, and their further growth into the lateral walls of the embryo and septum transversum will make them encircle the heart, thereby enlarging the pleuro-pericardial membranes and changing position of the phrenic nerves.

After the heart, lungs, liver and stomach are located in their permanent positions the pleuro-peritoneal membrane grows rapidly and soon closes the opening between the pleural and peritoneal cavities. Fig. 42 is from a section lateral to the opening showing the phrenic nerve throughout its greatest extent. In this specimen the marked growth is in the pleural cavity. Fig. 43 is from a section through the opening on a larger scale, including also the adrenal. A stage slightly more advanced is shown in Fig. 44. In this specimen, as in the one above, both pleural cavities communicate with the peritoneal. In Embryo LXXIV, Fig. 45, the pleuro-

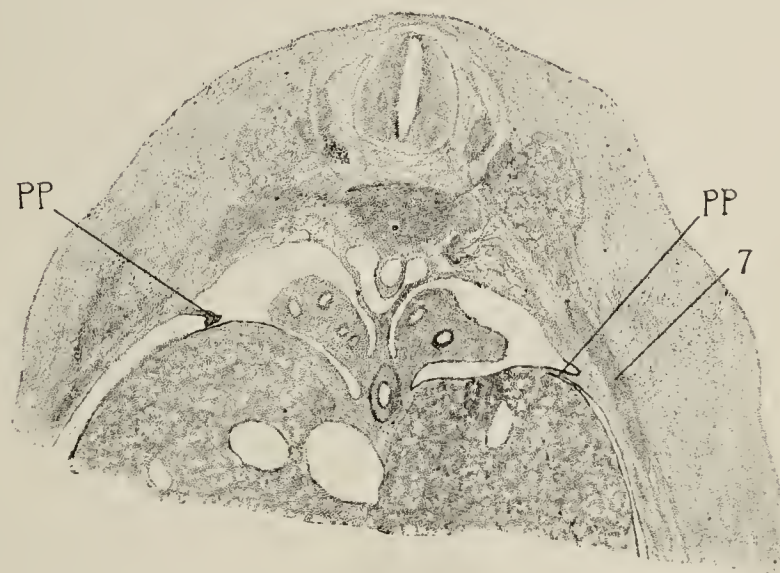


FIG. 45.—Transverse section through the embryo 14 mm. long. No. LXXIV \times 10 times; 7, seventh rib. The pleuro-peritoneal membrane; *pp*, is incomplete on one side.

peritoneal membrane is complete on the right side and incomplete on the left side. The reconstruction of this embryo shows that the opening is very large and extends from the seventh rib towards the tail. It may be an instance of retarded development, because in embryos 19 mm. long the membranes are as a rule complete on both sides of the body.

To what extent the permanent diaphragm is formed from the pleuro-peritoneal membrane it is difficult to determine. Undoubtedly the portion of the diaphragm on the caudal and dorsal sides of the pleuro-pericardial membrane is formed from the pleuro-peritoneal membrane. That portion of the diaphragm on the cephalic side is formed from the septum transversum. But the diaphragm is greatly extended on the lateral sides of the heart after the embryo is 20 mm. long by the extension of the pleural cavities around it. It appears from the models that this portion of the diaphragm is also formed directly from the periphery of the septum transversum.

OBSERVATIONS ON THE PECTORALIS MAJOR MUSCLE IN MAN.

BY WARREN HARMON LEWIS, M. D.,
Assistant in Anatomy, Johns Hopkins University.

THE ADULT MUSCLE.

The peculiar twist in the sternocostal portion of the pectoralis major muscle is described in the various text-books on human anatomy. In general, the descriptions would indicate that the posterior layer of the tendon of insertion is formed in such a manner that its highest fibres have the lowest origin on the thorax, and the lower the fibres at the insertion the higher their origin on the thorax. There must thus be a crossing of fibres. This crossing is generally represented as

direction of the fibres which form the apparent twisting. For this purpose specimens were taken from the dissecting room, from bodies embalmed with the carbolic acid mixture.¹ The muscles were placed in equal parts of glycerine, water and nitric acid for 24 to 48 hours. In most of the specimens thus treated the direction of the fibres was easily obtained as the connective-tissue elements were partially disintegrated and easily torn.

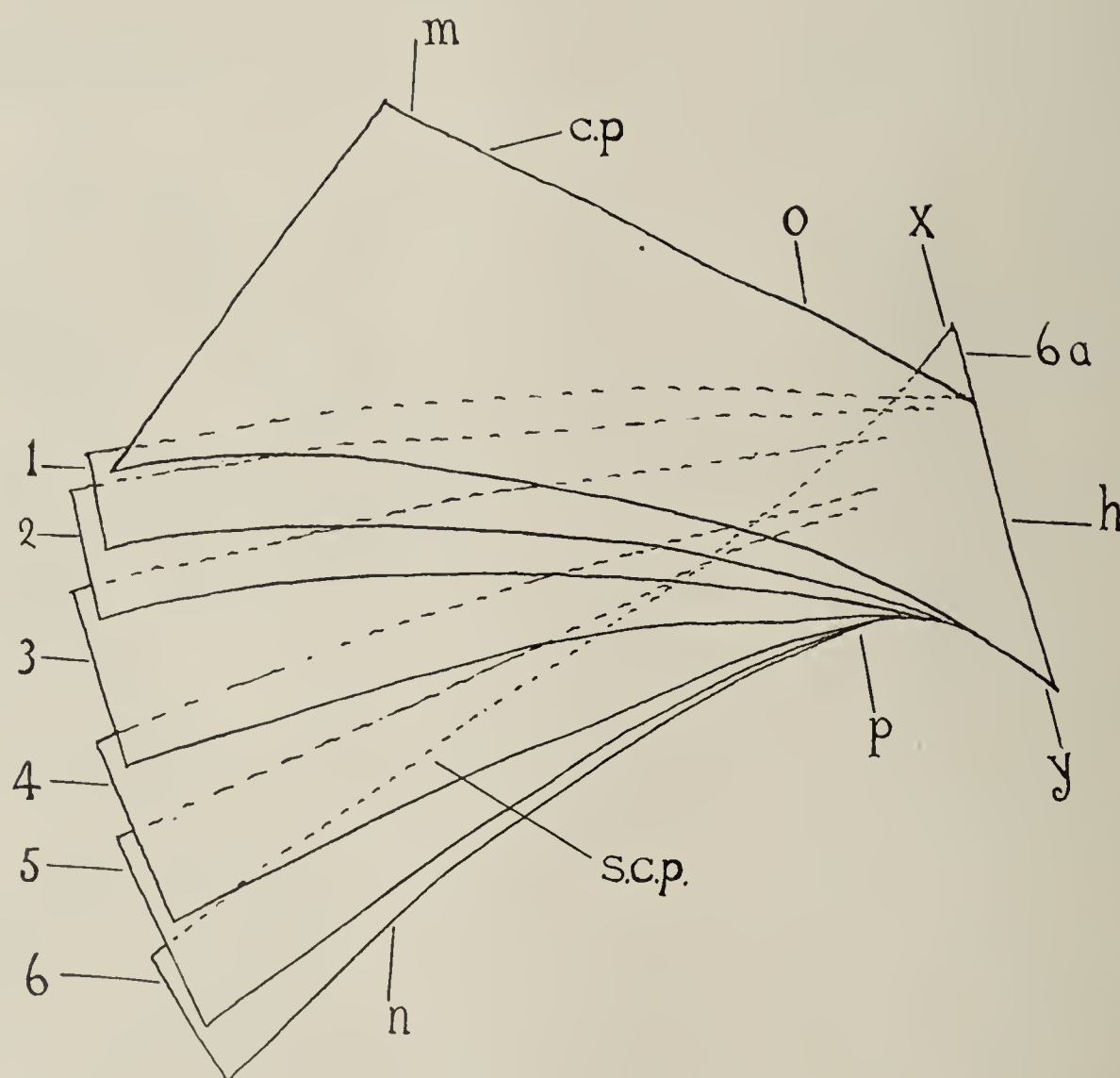


FIG. 1.—Diagram of an adult pectoralis major muscle. *c p*, clavicular portion; *s c p*, sternocostal portion; 1, 2, 3, 4, 5, 6, are overlapping bundles of fibres of the same; *6 a*, portion of the posterior layer of the tendon of insertion coming from 6; *h*, humeral end of the muscle.

taking place at or near the concave portion of the lower or axillary border of the muscle. I have found many anatomies incorrect or very incomplete in their description of the formation of the posterior layer of the tendon of insertion as well as the direction taken by the remaining sternocostal fibres, which go to the anterior layer of the tendon. These descriptions correspond fairly well with the direction the fibres appear to take when one examines the muscle superficially.

I have examined carefully twelve muscles to ascertain the

My dissections have shown in every case, (1) that the lowest fibres of origin go to the lowest end of the posterior layer of the tendon of insertion (Figs. 1 and 2), (2) that there is no crossing of fibres forming this posterior layer, and (3) that a peculiar fan-like arrangement of the bundles of fibres in the whole sternocostal portion is present (Figs. 1 and 2).

After the maceration, I found the muscle had a tendency

¹ F. P. Mall, *The Preservation of Anatomical Material for Dissection*, Anat. Anz., Bd. xi, p. 769, 1896.

to split into several overlapping bundles (Figs. 1 and 2; 1, 2, 3, 4, 5, 6). The number and size varies in different museles. It will be seen from the diagram (Figs. 1 and 2) that the overlapping is more and more marked toward the humeral insertion.

The clavicular portion and upper five bundles form the anterior layer, and the sixth bundle the posterior layer, of the tendon of insertion. The lower fibres in each bundle, which are the superficial overlapping ones, reach to the lower end of the tendon, while the upper, deeper ones are more and more overlapped and pass to the upper edge or near to the upper edge of the tendon. Each bundle, as it approaches the tendon of insertion, spreads out and becomes thinner.

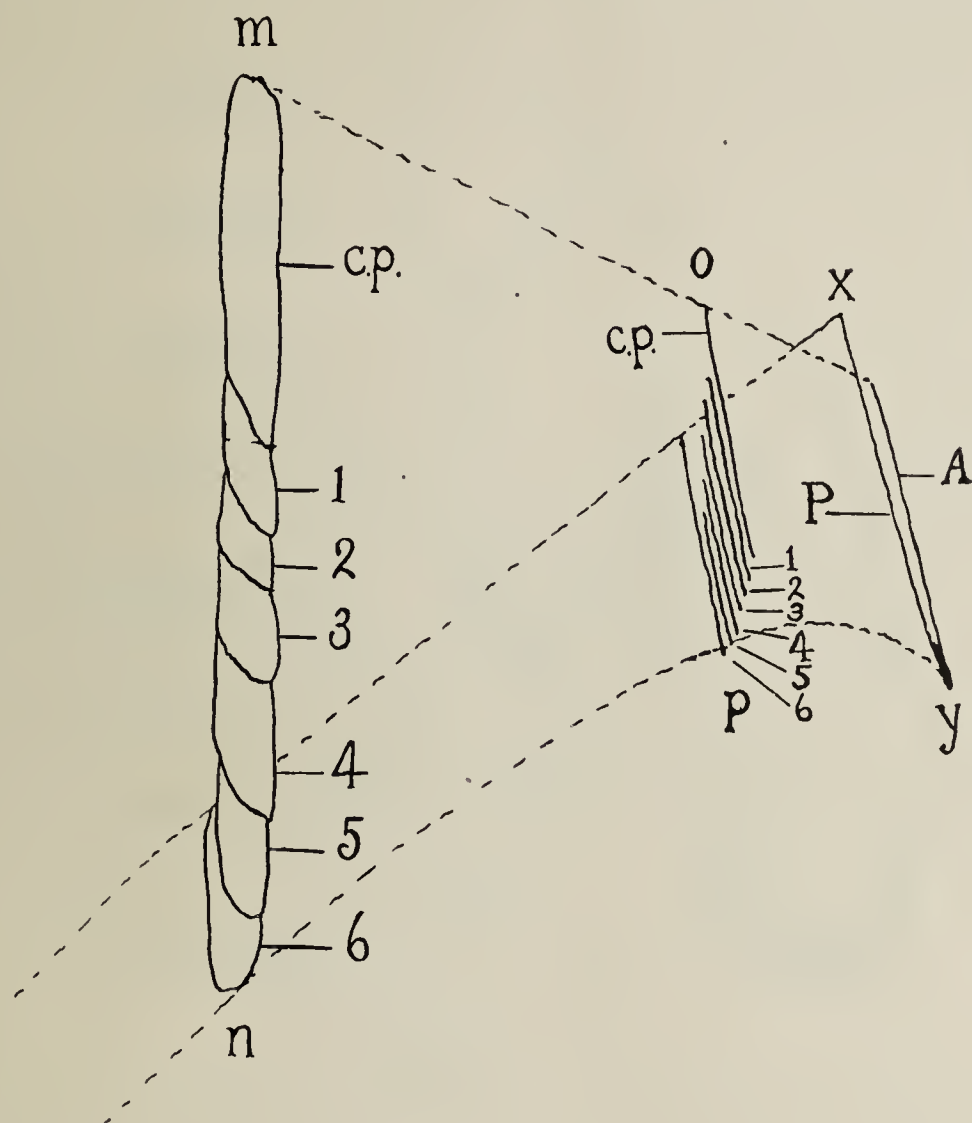


FIG. 2.—Diagram of cross-sections of the musele taken at *mn*; *op*; and *xy*, in (Fig. 1). Numbers and letters remain as Fig. 1. *A*, anterior layer of tendon; *P*, posterior layer.

The distance to which the musele fibres go outward toward the humerus decreases from above downward and thus aids in keeping the distal end of the musele thin.

The posterior layer of the tendon is continuous with bundle 6 (Figs. 1 and 2). It gradually spreads out and becomes thinner on approaching the humerus. As in the other bundles, its lower fibres reach the lower and its upper fibres the upper border of the tendon. The size of this bundle varies greatly, especially in the amount of overlapping toward the origin. Most of its fibres constitute the abdominal portion to which the musele is sometimes divided. The accessory bundles of musele having, as a rule, costal origin and which are beneath the main musele, are inserted into this posterior layer.

DEVELOPMENT.

I have attempted to trace the development of the musele in a series of human embryos and to explain the origin of the peculiar arrangement of its fibres. For this purpose I have studied the musele carefully in embryos varying in length from 9 to 40 mm. The first indication of the musele I have been able to note was in an embryo of 9 mm. in length. In an embryo of 40 mm. the adult form is present. Reconstructions of the younger and dissections of the older embryos were made to study them.

In a human embryo measuring 9 mm. in length (No. CLXIII),² the pectoralis major and minor museles are repre-

sented by a mass of closely packed cells without sharp limits. As there are no musele fibres in this tissue I shall call it pre-musele tissue. The other muscles of the arm and shoulder girdle are also represented more or less clearly by this pre-musele tissue. There are, however, musele fibres in the musele-plate system. Here the musele plates have fused into a continuous column and in the costal region extend along the intercostal spaces, partially surrounding the ribs and fuse together beyond their tips into a ventral plate. This musele-plate system contains fibres, is farther advanced

² The numbers here given correspond with those in the catalogue of the collection of human embryos in the Anatomical Laboratory of the Johns Hopkins University.

and has a different appearance from the premuscle tissue, which is lateral to it and in the arm. In Fig. 3, which is from a wax reconstruction of the right arm region of this embryo, the costal portion of the muscle-plate system is seen (*m.pl.s.*). Lateral to this is the lateral premuscle mass (*l.pm.*). At the level of the first rib (*cI.*) the pectoral premuscle mass (*p.pm.*) leaves the lateral to join the general arm premuscle sheath (*a.pm.*) along the ventral side of the proximal half of the condensed tissue which represents the humerus. The proximal end of the humerus lies opposite the interval between the fifth and sixth intervertebral disks (*dVc, dVIc*), the distal end opposite the first rib (*cI.*). The

tion into masses, such as the pectoral, latissimus dorsi and levator scapulae and serratus anterior. It is impossible for me in the case of the pectoral mass to determine how far caudally into the lateral premuscle tissue it extends, or just where to draw the line between it and the neck premuscle mass. Its humeral end is lost in the general arm premuscle tissue. Its location and correspondence with the muscle in the next stage and its nerve supply lead me to believe this to be the pectoral mass.

The pectoral premuscle mass is supplied by three nerves, from the brachial plexus, the fibres of which come from the VI, VII and VIII cervical and I thoracic nerves. It will

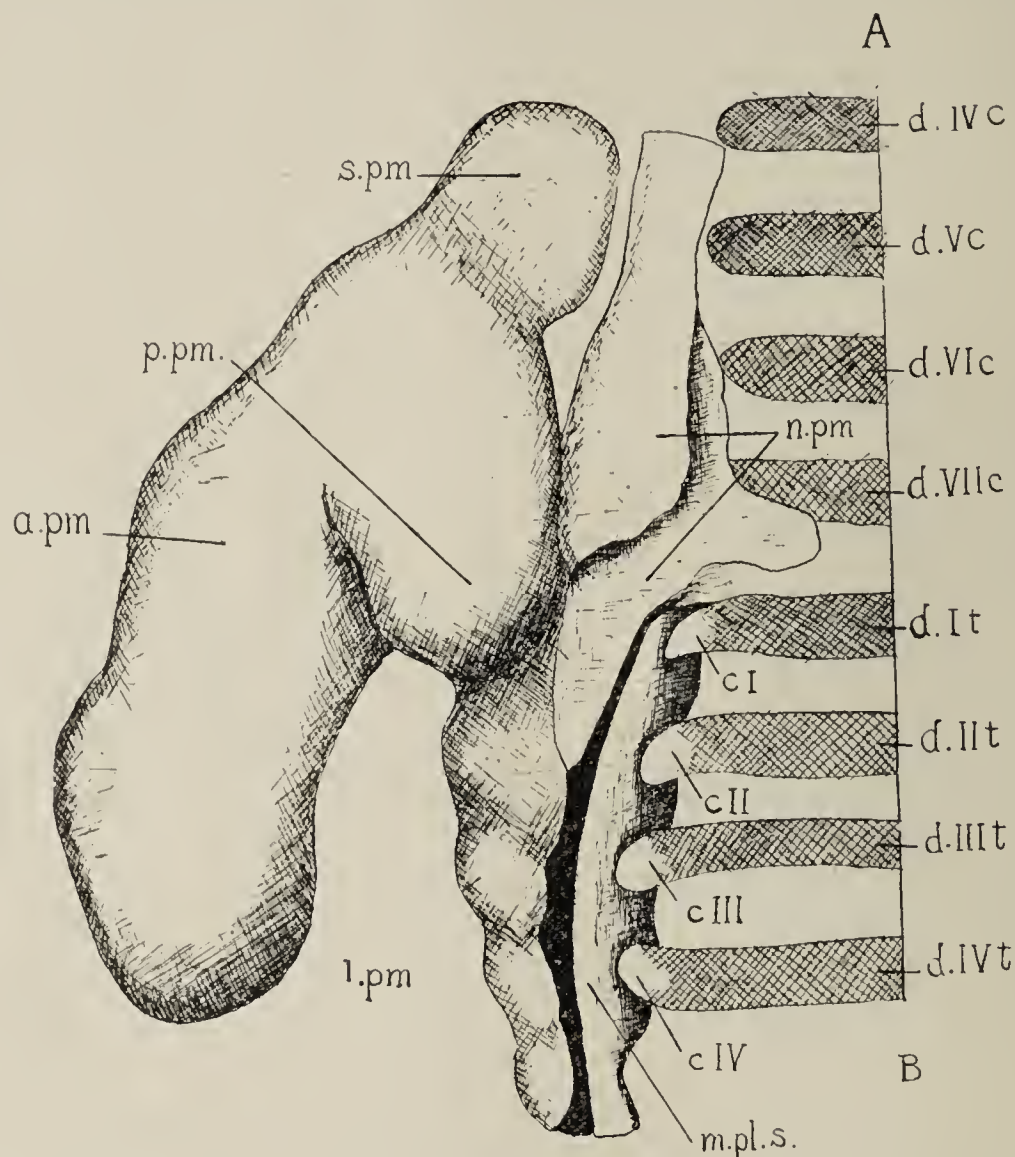


FIG. 3.—Ventral view of a wax reconstruction of the arm region of a human embryo measuring 9 mm. in length (No. CLXIII). Enlarged 50 times. *AB*, median line; *cI, cII, cIII, cIV*, ribs one, two, three and four; *dIVc, dVc, dVIc, dVIIc*, fourth, fifth, sixth and seventh cervical intervertebral disks; *a.pm*, premuscle mass ensheathing the arm; *l.pm*, lateral premuscle mass; *p.pm*, pectoral premuscle mass; *s.pm*, scapular premuscle mass.

scapula lies imbedded in the scapular premuscle tissue (*s.pm.*). The clavicle is not present at this stage. The intervertebral disks are of condensed or closely packed cellular tissue (*dIVc*, etc., to *dIVt*). The ribs are of condensed tissue and project ventrad from the adjoining parts of the intervertebral disks and vertebral bows.

It is very difficult to determine the exact limits of the premuscle tissue; in a few places it is very sharply marked off from the surrounding mesenchyma as at the ventral end of the neck premuscle mass. The entire arm between the central skeletal core and the integument is filled with this tissue. At the root of the arm there are signs of a separa-

be seen at this stage that the pectoral mass is mostly cervical and lies in the region of its nerve supply.

The fibres of the brachial plexus are directed laterally and have scarcely any caudal inclination.

In an embryo measuring 11 mm. in length (No. CIX),³ there is great advance in the musculature of the arm. Many of the arm muscles, especially the proximal ones, can be

³ Mall, (F.). The value of Embryological Specimens, Maryland Med. Journal, October 29, 1898. A Contribution to the Study of the Pathology of Early Human Embryos. Contributions to the Science of Medicine, dedicated to William H. Welch, Johns Hopkins Hospital Reports, vol. ix, 1900.

recognized. Instead of pre-muscle tissue we have distinct fibrillation.

The pectoral muscle mass extends from the region lateral to the ends of the first three ribs cephalolaterad to the cephalic border of the humerus. Its cephalic portion is closely associated with the medial end of the clavicle (Figs. 4 and 5, *cp.*). There is no definite attachment of the muscle to the ribs. The pectoralis major and minor are closely united. The latter is indicated by a bulging toward the coracoid process (*p.min.*, Figs. 4 and 5). I have with difficulty traced the general course of the fibres in the major portion of the mass, as will be seen in Fig. 5. The fibres from the clavicle do not appear to overlap the sternocostal fibres but occupy the proximal part of the insertion, while the sternocostal fibres occupy the distal. See Fig. 6, which is a diagram of the relation of these fibres close to their insertion into the humerus.

It is also worthy of note that the pectoralis muscle has extended caudally to the level of the tip of the third rib.

In an embryo measuring 16 mm. in length (No. XLIII),⁴ the two pectoral muscles are entirely separate. The pectoralis major muscle assumes much more the adult form than in the previous stage. The entire arm has migrated caudally and with it the pectoralis major muscle. It now extends to the sixth rib (Fig. 7, *cVI.*). The clavicle has extended to the tip of the first rib, where it joins the cephalic end of the sternal anlage (*st.*, Fig. 7). The clavicular portion of the muscles is carried with the clavicle toward the median line. The humeral end of its fibres are seen to overlap the sternocostal fibres near the humerus (Figs. 7 and 8). There is a distinct gap between the clavicular portion (Fig. 7, *cp.*) and the sternocostal portion (Fig. 7, *scp.*) near their origins. The fibres of the sternocostal portion present a slight tendency to separate into bundles in which there is an overlap-

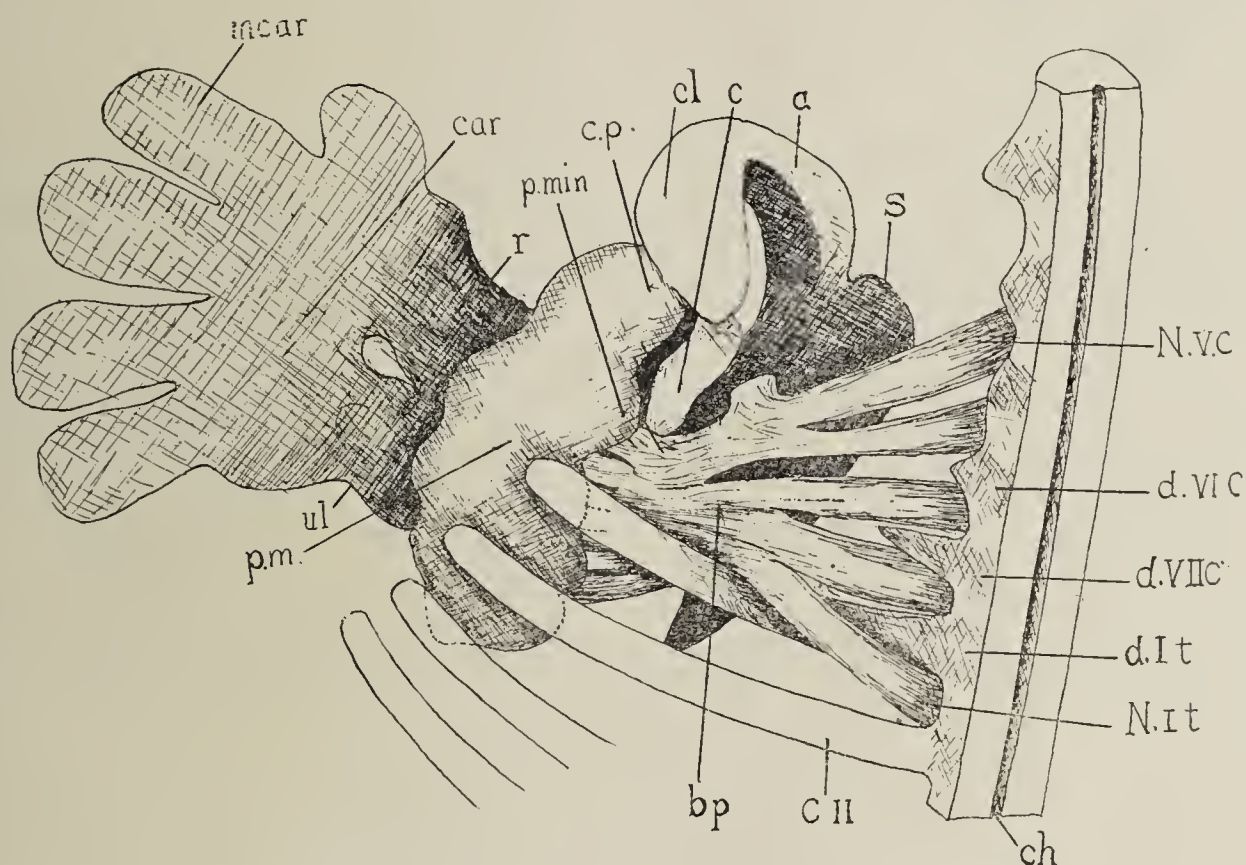


FIG. 4.—Median view of a wax reconstruction of the arm region of a human embryo measuring 11 mm. in length (No. CIX). Enlarged 30 times. *A*, acromion; *c II*, second rib; *c*, coracoid process; *car*, carpus; *c p.*, clavicular portion of the pectoralis major; *cl*, clavicle; *ch*, chorda dorsalis split in the median line; *d VI c*, *d VII c*, sixth and seventh cervical intervertebral disks; *d I t*, first thoracic intervertebral disk, from which the first rib is seen arising; *mcar*, metacarpus; *p. m.*, pectoralis major muscle; *p. min.*, pectoralis minor bulging toward the coracoid process; *n, V c*, fifth cervical nerve going to join the brachial plexus; *bp*, brachial plexus; *r*, radius; *ul*, ulna; *s*, scapula.

Figures 4 and 5 are from a wax reconstruction of the right arm region of this embryo. All muscles but the pectorals are omitted.

The pectoral muscle mass is supplied by four branches of the brachial plexus, two from the outer and two from the inner cord, the fibres of which can be traced to the *VI*, *VII* and *VIII* cervical and *I* thoracic nerves.

It is of special note at this stage, that the larger portion of the muscle lies above the first rib, reaching about to the level of the fifth cervical intervertebral disk; that there is no overlapping of its fibres; and that the clavicle only reaches about one-half the distance from the acromion to the first rib.

ping of the deep portion of the lower by the superficial portion of the upper ones. This is more marked toward the insertion, as will be seen in Fig. 8, where the overlapping is quite complete. I have not been able to make out at this stage anything which corresponds to the deep or posterior tendon and, as will be seen later, it probably does not exist at this stage.

⁴ Mall, (F). Development of the Human Cœlom, Jour. of Morph., vol. xii, No. 2. Development of the Internal Mammary and Deep Epigastric Arteries in Man, Johns Hopkins Hospital Bulletin, Nos. 90-91, 1898. Development of the Ventral Abdominal Walls in Man, Jour. of Morph., vol. xiv, No. 2, 1898.

The nerve supply is as in the adult.

Embryo No. XXII,⁵ measuring 20 mm. in length, shows about the same condition as in Embryo No. XLIII. The separation of the sternocostal portion into various bundles is especially well marked. They have no relation to the ribs so far as the number and position is concerned.

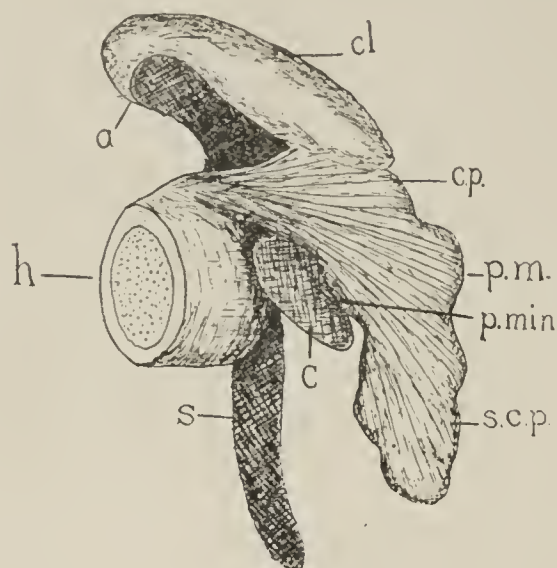


FIG. 5.—Ventral view of a portion of the model shown in Fig. 4, showing the pectoral muscle mass and its relations to the scapula, clavicle and humerus. *a*, acromion; *c*, coracoid process; *cl*, clavicle; *h*, humerus; *p. m.*, pectoral muscle mass; *cp*, clavicular portion; *s c p*, sternocostal portion; *p. min*, pectoralis minor bulging; *s*, scapula.

In an embryo 32 mm. in length (No. CXXIX),⁶ we find that the posterior layer of the tendon of insertion has made its appearance (Fig. 9). The fibres which go to this tendon come from the most caudal portion of the muscle. This posterior layer is about one-fourth the width of the anterior layer of the tendon of insertion. The embryo was studied with a dissecting microscope and so far I could determine

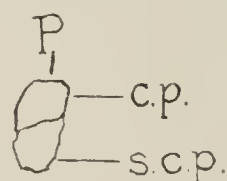


Fig 6.—Diagram of a cross-section of the pectoralis major fibres near their humeral insertion. Enlarged 50 times. *P*, proximal end of the same; *c p*, clavicular fibres; *s c p*, sternocostal fibres.

the arrangement of its fibres was otherwise similar to the adult.

In an embryo 36 mm. in length (No. XC), we find the posterior layer of the tendon of insertion nearly three-fourths the length of the anterior (Fig. 10). Otherwise the muscle appears to be much as in the adult. The pectoral region was studied with a dissecting microscope.

⁵ Mall, Maryland Medical Jour., October 29, 1898. Ibid., Jour. Morph., vol. xiv, No. 2, 1898. Ibid., Johns Hopkins Hospital Reports, vol. ix, 1900.

⁶ Mall, Contributions to the Science of Medicine, dedicated to William H. Welch, Baltimore, 1900, Johns Hopkins Hospital Reports, vol. ix, 1900.

In an embryo of 40 mm. in length the posterior layer of the tendon exceeds the anterior in width, and the muscle presents the adult form.

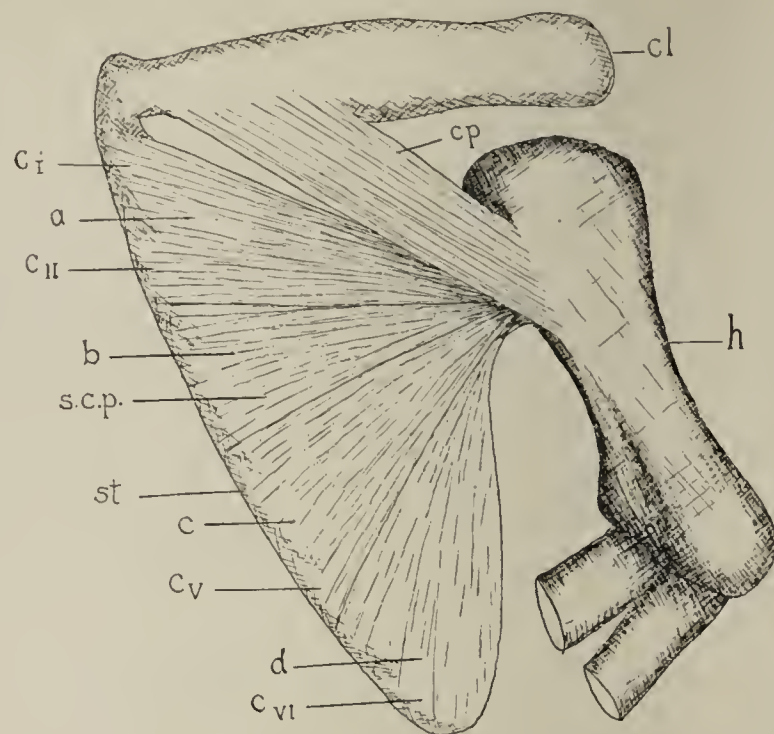


FIG. 7.—Ventral view of the pectoralis major muscle in an embryo measuring 16 mm. in length (No. XLIII), taken from a wax reconstruction of the arm region of the same. Enlarged 30 times. *s c p*, sternocostal portion, various artificial divisions of which *a*, *b*, *c*, *d*, are shown near their insertion in Fig. 8; *c I*, *c II*, *c V*, *c VI*, ends of first, second, fifth and sixth ribs, which, with the third and fourth join together to form the left half of the pectoralis major muscle; *h*, humerus, *p. m.*, pectoral muscle mass; *s c p*, sternocostal portion; *s*, body of the scapula; *st*, sternum; *c p*, clavicular portion; *cl*, clavicle; *h*, humerus.

SUMMARY.

It is thus seen that the pectoralis major muscle arises in common with the minor from a premuscle tissue which is

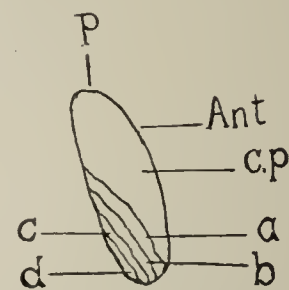


FIG. 8.—Diagram of cross-section of the pectoralis major muscle seen in Fig. 7, near its insertion into the humerus. Enlarged 30 times. *P*, proximal; *ant*, ventral surface; *c p*, clavicular portion; *a*, *b*, *c*, approximate position of the corresponding muscle bundles of Fig. 7.

located for the most part above the first rib. It gradually migrates or shifts to the costal region, as has already been noted by Dr. Mall.⁷ During the course of this migration it splits into bundles. The clavicular portion is the first to split off. Later the sternocostal portion splits into the major

⁷ Mall, Development of the Ventral Abdominal Walls in Man. Jour. of Morph., vol. xiv, No. 2, 1898.

and minor. The major becomes arranged into a series of overlapping bundles. As we have seen, the clavicular portion is the upper and most superficial. During the migration the overlapping of the sternocostal bundles is such that superficial fibres of each bundle have descended farther than the deeper, owing perhaps to the greater friction of the

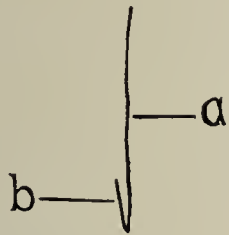


FIG. 9.—Diagram of the insertion of the pectoralis major muscle in an embryo 30 mm. in length (No. CXXIX). Enlarged 16 times. *A*, anterior layer of the tendon; *b*, posterior layer.

latter against the chest wall or to their earlier attachment. The lower bundle seems to be the last to be differentiated, and its tendon, the posterior layer of the tendon of insertion, appears to gradually spread out toward the proximal end of the humerus after the superficial or anterior layer is well formed.

The early entrance of the nerves into the muscle while still in the cervical region explains the adult nerve supply.

EXPLANATION OF VARIETIES.

It would seem that in the conditions existing between an embryo of 9 and 11 mm. in length might be found a partial explanation of such varieties as absence of the sternocostal or clavicular portions and of the pectoralis minor with the sternocostal portion. We have here a condition in which

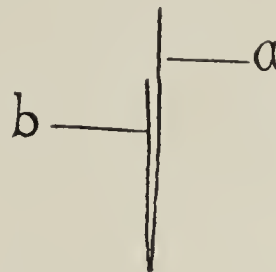


FIG. 10.—Diagram of the tendon near its insertion of the pectoralis major muscle of an embryo 36 mm. in length (No. XC). Enlarged 16 times. *A*, anterior layer; *b*, posterior layer.

the clavicle is absent and no attachment to the ribs exists. The subsequent attachment to one or the other might not occur and that portion of the muscle found wanting in the adult. With absence of the sternocostal portion would be associated that of the pectoralis minor owing to their early fusion. In the tendency to split into bundles, with the shifting of the muscle and fibres, the muscular bands which are often found as the costocoracoides, sternalis, chondroepitrochlearis, etc., may have their origin.

ON THE BLOOD-VESSELS OF THE HUMAN LYMPHATIC GLAND.

BY W. J. CALVERT, M. D., U. S. A.,

Pathological Laboratory, Board of Health, Manila, P. I.

The lymphatic glands removed at autopsy from pest cadavers have enabled me, on account of the extreme congestion incidental to the disease and the reduction in the density of the nuclear elements of the gland, to follow in detail the course of the smaller vessels; the pathological changes referred to are not of sufficient degree to destroy the landmarks of the organ or to change the general relationship of the parts.

In an earlier communication I showed the course of the blood-vessels in the lymph follicle in the dog, and the present report is made because it demonstrates that the same arrangement is present in the human lymphatic gland.

The glands were fixed in Zenker's fluid, hardened in alcohol, sectioned in celloidin, stained in hæmatoxylin and eosin and mounted in balsam.

The illustrations show the origin and distribution of the follicular artery, the arrangement of the capillaries in the follicle and the origin of the veins. The course of the

arteriæ and venæ lympho-glandulæ and the vessels of the cord have been illustrated.¹

From the above illustrations and the many typical pictures seen in the slides the following scheme for the blood supply of the human lymphatic gland may be described: The arteriæ lympho-glandulæ enter the gland at the hilus, pass through the hilus stroma to enter the trabeculæ. In the trabeculæ arterial twigs are distributed to all portions of the gland. On reaching the portions of the gland near the proximal ends of the follicles small arteries arise which run in the lymphatic structure more or less parallel to the surface of the gland. These arteries give rise to the follicular artery (Figs. 1 and 2) and supply the adjacent portions of the pulp cords.

The follicular artery runs a straight course in or near

¹ The Blood-vessels of the Lymphatic Gland. By W. J. Calvert *Anatomischer Anzeiger*, xiii. Band, Nr. 6, 1897, p. 176.

the centre of the lymph cord of its particular follicle, to about the junction of the proximal with the middle third of the follicle. The follicular artery may give off branches to supply the adjacent portions of the cords. Near the centre of the follicle the artery breaks up into a number of small, straight, long capillaries which diverge to the periphery of the follicle. In some cases these capillaries branch, in others they do not.

Just beneath the periphery of the follicle these capillaries turn and branching form a rich plexus of capillaries which in turn unite to form small veins (Fig. 6). The plexus of capillaries in the follicle is continuous with a similar plexus in the cords.

The veins formed in the follicle run toward the proximal end of the follicle to join a rich plexus of veins.

The arteries supplying the cords are, as a rule, quite short,

run in or near the centre of the cords and rapidly end in a rich capillary plexus near the surface of the cord. This plexus soon unites to form small veins which also run in or near the centre of the cords, but in a portion of the cord other than where the artery is found. The veins of the cord soon join veins from neighboring cords, through the anastomosis of the cords, to form larger veins which leave the cords to join the *venæ lympho-glandulæ*.

The veins from the follicles and adjacent portions of the cords unite to form a rich venous plexus, which lies within the lymphatic structure. This plexus may be considered to be the origin of the *venæ lympho-glandulæ*, which, like the arteries, run in the trabeculæ to leave the gland at the hilus.

The lymph channels are free from blood-vessels.

This arrangement of blood-vessels is also found in the lymph gland of the monkey.

NORMAL MENSTRUATION AND SOME OF THE FACTORS MODIFYING IT.

(PRELIMINARY NOTE.)

By CLELIA DUEL MOSHER, A. M., M. D.,

Gynecological Externe in the Johns Hopkins Hospital Dispensary.

The conclusions stated in this note are based on two kinds of data—clinical and experimental. The first consists of serial menstrual records of more than 300 women, collectively extending over more than 3000 menstrual periods. A large number of these records were made by the writer, month by month, when the women were under her personal observation in the Stanford University Gymnasium, and then were continued by the women themselves during holidays and vacations away from the university. The records were supplemented by preliminary statements, careful intermenstrual notes, and subsequent letters. The usual physical examination for admission to the gymnasium was made by the writer in many cases; to this was added an intimate knowledge of the conditions under which the women were living and working. Second, laboratory experimental data on the respiration,¹ urine, temperature, pulse and blood—blood pressure, blood counts, hemoglobin estimations and so on. Experimental work on the effects of clothing was also included. This work has been done in the physiological laboratories of the Stanford and the Johns Hopkins Universities, and in Dr. Kelly's laboratory. The first work was done in May, 1893, in California, has been continued as opportunity offered and is still in progress.

Some of the more important conclusions, which are based largely on the blood-pressure experiments and clinical data will be reported at this time.

Method.—Daily records of the blood pressure were made on 14 persons—9 women and 5 men. The women were selected as representing normal conditions of menstrual health. The men were all healthy adults and 4 were athletic. An attempt was made to continue the records long enough to cover at least two periods of change in pressure; in some cases the observations extended over 49 days and some are still in progress. The blood-pressure records were made with the sphygmomanometer of Mosso. The tracings were taken daily at the same hour and under uniform conditions, perfect relaxation being secured and all variable factors excluded as far as possible.

Conclusions.—That a rhythmical fall of blood pressure, at definite intervals, occurs in both men and women. The daily records of the blood-pressure with the sphygmomanometer of Mosso on men and women under similar conditions of life and occupation give curves apparently indistinguishable in character. The fall in pressure in women occurs near or at the menstrual period. In all of the 14 series of records the fall of blood-pressure was gradual from the mean average pressure. This from day to day shows oscillations within rather definite limits. The maximum fall of pressure may extend over two or three days and the corresponding rise to the normal average pressure is gradual. There is usually a preliminary rise, above the normal average pressure; this occurs from 3 to 5 days before the onset of the main fall of pressure, which constitutes the principal feature of the rhythm. In every case there was a preliminary fall, abrupt and definite, but usually not so extensive as the main fall of pressure; this preliminary fall was followed by

¹ "Respiration in Women," Preliminary report as thesis for M. A. degree, Stanford University, May, 1894. Also paper presented at California Science Association, Jan. 3, 1896.

FIG. 1.—The follicular artery and its capillaries. One of the long capillaries is seen to join a venous capillary in the periphery of the follicle; on either side of the follicle small veins are seen. Transverse sections of several veins are also seen.

Measurements: artery before dividing, 41 microns; and capillaries from 8 to 10 microns in diameter



FIG. 2.—The origin, course and distribution of a long follicular artery.

Measurements: at origin, 54 microns; and before dividing, 31 microns; capillaries in follicle, from 7 to 8 microns.

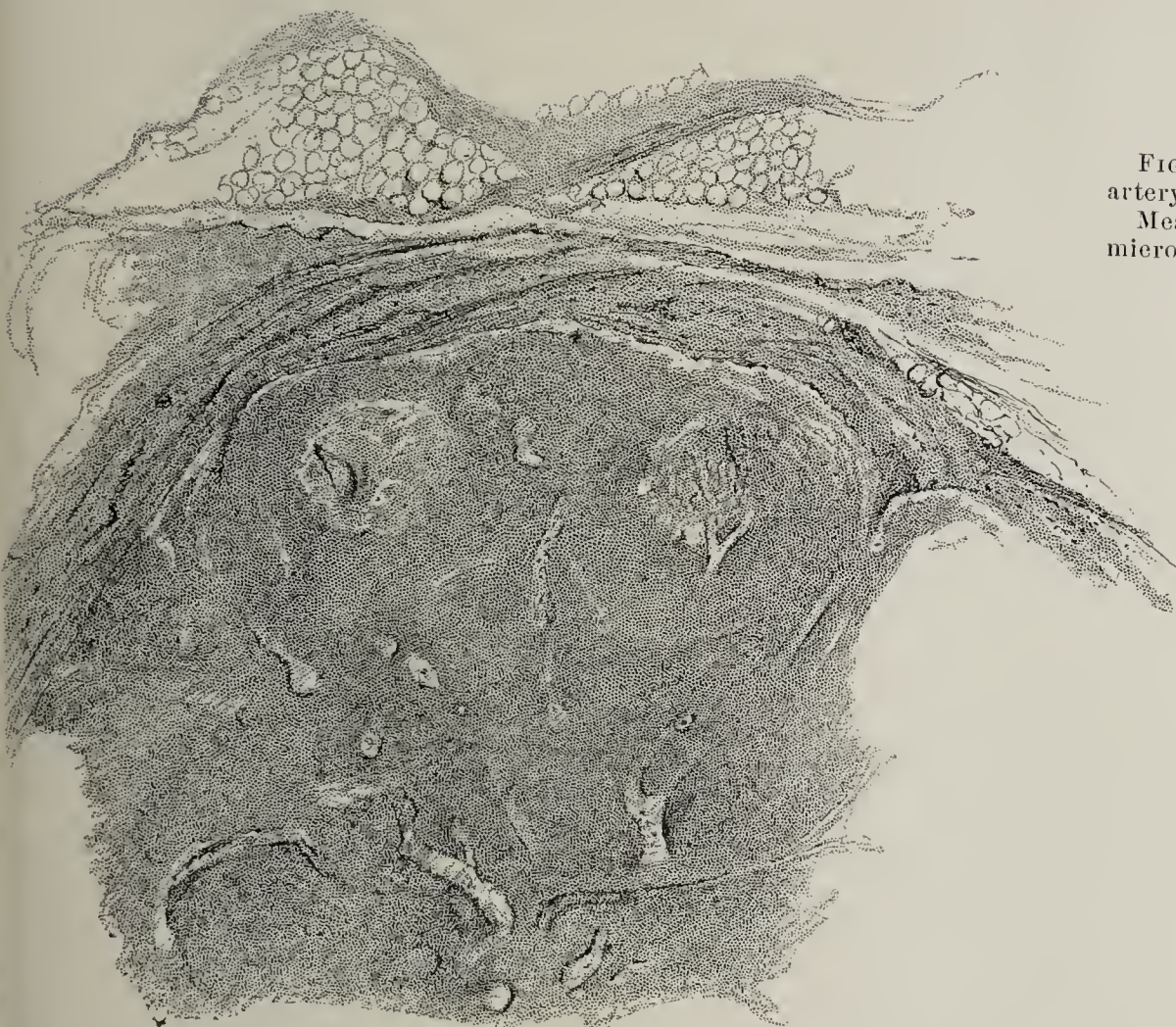


FIG. 5.—Two follicles with their veins. The follicle on the right shows a portion of a follicular artery entering the centre of the follicle. Below the proximal end of the follicle an artery is seen running parallel to the surface of the gland to turn toward the proximal end of the follicle; here it is lost.

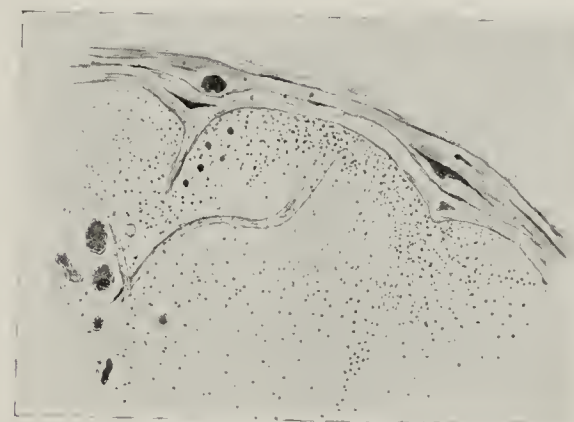


FIG. 3.—An artery arising some distance below the proximal end of a follicle, running toward the follicle to turn at a right angle and run to the centre of the proximal end of the follicle; here it again turns at a right angle to enter the follicle, where it divides in the usual manner.



FIG. 6.—Long curved capillaries, c, near the periphery of the follicle.

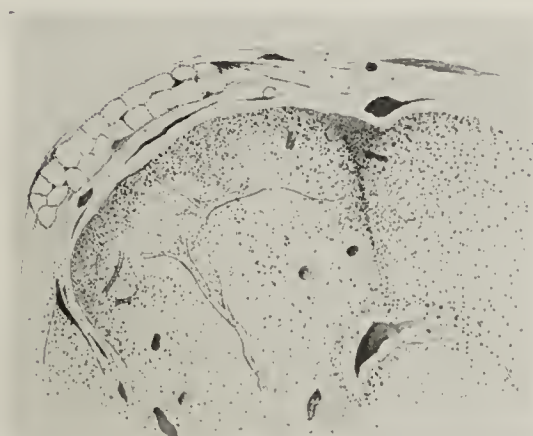


FIG. 4.—A double arterial supply to the follicle.

a return to the normal or higher pressure before the principal fall occurred. In 4 cases there was a distinct rise above normal after the main fall of pressure before the return to the normal daily oscillations. These variations were not peculiar to either sex.

A curve constructed on the subjective observations of the sense of well being, shows ups and downs corresponding to the marked variations in pressure; the sense of maximum efficiency of the individual corresponding to the time when the pressure is high, and lessened efficiency to the periods of low pressure. The observations were carried on independently of each other. In no case was the change sufficient to incapacitate the individual. The time of low pressure appears to be, in both sexes, a period of increased susceptibility. If symptoms of any kind are shown they are apt to be given by the point of least resistance. For example, if a man or woman having a tendency to digestive disturbances, the symptoms from the digestive tract are likely to occur at the period of low blood pressure; or when a slight chronic catarrh exists, as so frequently happens in this climate, there may be marked increase of symptoms from the respiratory tract.

In women the fall in blood pressure most frequently occurs before the menstrual flow, the maximum fall being coincident with the onset of the flow; there is a gradual return to the normal mean pressure by the time the menstruation ceases. Occasionally the fall occurred during the flow.

While true dysmenorrhœa is far too frequent, much of the so-called menstrual suffering is not dysmenorrhœa but simply coincident functional disturbances in other organs, induced, possibly, by the favoring conditions of a lowered general blood pressure occurring near or at the time of menstruation. (Goodman's restricted definition of menstruation is adhered to—"A periodic sanguineous defluxion from the genital tract.")

When the attention is of necessity directed to so obvious a

process as the menstrual flow, untrained women, especially if without absorbing occupation, naturally refer their lessened sense of well being and diminished sense of efficiency, which may accompany the lowered general blood pressure occurring near or at the menstrual flow, to the function of menstruation. When we remember how firmly fixed is the tradition that a woman must suffer and be incapacitated by this normal physiological function, it is readily understood how many women would call the depression due to lowered blood pressure, menstrual suffering.

All statistics, however extensive or carefully taken, are likely to exaggerate the percentage of women suffering from dysmenorrhœa, because the errors just mentioned are so difficult to eliminate.

The conception that functional disturbances in other organs are considered and recorded as dysmenorrhœa was first derived from the study of the clinical data and later strengthened by the blood-pressure experiments supplemented by the notes of the persons studied.

The conclusions of this paper would have been impossible had my clinical data consisted merely of isolated statements based on the general impressions, as to their own conditions, of individual women filling out a single menstrual record, and without a personal acquaintance with, and an intimate knowledge of, the habits of life and conditions of work of the women studied.

Although space forbids detailed acknowledgements at this time, I wish to state my obligations for many favors received at Stanford University in the earlier work; to Dr. Howell and his associates, Dr. Dawson and Dr. Erlanger of the Physiological Department of the Johns Hopkins University; to Dr. Kelly's liberality and generous encouragement which have made possible all of the later work. The intelligent cooperation of my former students and many friends and of the men and women who have recently given and are giving so much of their valuable time, has made this work possible.

RETROJECTION OF BILE INTO THE PANCREAS, A CAUSE OF ACUTE HEMORRHAGIC PANCREATITIS.

BY W. S. HALSTED, M. D.

Mr. T., aged 48, a corpulent and robust looking man, had been subject to attacks of "indigestion," attended with pain in the epigastrium and a feeling of distention, for several years. These attacks would sometimes incapacitate him for business. He had a severe attack of this kind last Christmas. He described also attacks of "vertigo," which had laid him up for 8 or 10 days every spring, with perhaps one exception, for the past ten years. At the end of April, 1901, he arrived in Baltimore after a hard railroad trip of about 5 days. On the way, suffering with indigestion, he bought a two-ounce package of bicarbonate of soda, half of which he consumed. After luncheon on the day of his arrival he

was seized quite suddenly with a severe pain in the abdomen; he was nauseated and expressed his desire to be relieved of the "gas in the stomach." His physician administered calomel, and later nux vomica and carminatives. For 24 hours he was relieved; then, after eating buckwheat cakes, the pain returned. Occasionally drinking large quantities of water, he forced himself with difficulty to vomit. He suffered almost constantly more or less pain for a week, but took his meals regularly and slept about as well as usual. About noon on the 5th of May, the pain became very severe; morphia administered hypodermically three times during the afternoon, $\frac{1}{2}$ grain in all, did not give much relief.

Inhalations of chloroform had to be given. At 9 p. m. I was asked to see him by his attending physicians. As I entered his bedroom, he was walking about in his pajamas, excited and nervous, and his teeth chattering; he seemed to be in great pain. His pulse was full and regular, 92 the first count and 87 the second. When I attempted to examine him he made an effort to keep quiet but in a moment had to spring up again. He was sensitive to pressure over the epigastrium, but not exquisitely, the point of greatest tenderness being a little above and, I thought, to the right of the umbilicus. He was somewhat cyanosed. My attention was called to the cyanosis by the print of my fingers on his abdominal wall. His condition was so good that I thought, with his physicians, he was probably suffering from gall stones. He refused to go to the hospital. Hot baths during the night relieved him, I am told, for the time, but he had to be chloroformed frequently. In the morning he was anxious to go to the hospital and was operated upon immediately after his arrival, about 11 a. m.

Operation.—The cyanosis of the patient was much more striking as he was laid on the operating table, and he vomited as he was being anesthetized. The abdomen was not distended, but the panniculus was very deep. On opening the belly through the middle line blood-stained fluid escaped and at once it was noticed that the omentum showed abundant fat necroses; these necroses were to be seen in the subperitoneal fat, in the mesentery, along the lesser and greater curvatures of the stomach, etc. In order to explore more fully the pancreas and to make sure that a certain hemorrhage in the wall of the stomach, near the pyloric end, had not produced any serious lesion, the omental bursa was rapidly opened. Nothing that could be designated as a tumor mass was made out; the entire region of the pancreas could be palpated. The tissues over the pancreas were slightly infiltrated with blood-stained serum. The common bile duct, however, was distended to the size, perhaps, of an index finger. The presence of a stone in the diverticulum was of course suspected, and a careful though hurried search made, but none could be felt; the fluid in the abdominal cavity was rapidly sponged out and a gauze pack placed over the head of the pancreas. The abdomen was then closed. The patient died within 23 hours.

Pain, vomiting, distention of the abdomen, sometimes an elastic swelling in the region of the pancreas, fluid in the peritoneal cavity, pulse 140 to 160 or higher, cyanosis, collapse—these are the symptoms which the surgeon calls to mind when he pictures to himself a case of acute hemorrhagic pancreatitis, and hence it is that this disease has so many times been considered acute intestinal obstruction. My patient was strong, restless and walking about the room, not collapsed; his pulse was 92 the first count, 87 the second; the abdomen was not only not distended but, according to the patient, had greatly diminished in size during the few weeks preceding this illness; the reduction in the size of his waist, as evidenced by the considerable space between the band of his trousers and his abdominal wall, was a matter

which apparently gave him some concern, for he referred to it more than once. Vomiting, if present, was so inconspicuous a symptom that it had not been noticed; the patient had perhaps 3 or 4 times tickled his pharynx because he thought it relieved him to gag and bring up a little mucus from his stomach. When I saw him about 13 hours before the operation and again an hour before it, pain in the epigastrium and slight cyanosis were his only symptoms. But the pain must have been intense and seemed greater than I had ever seen it in cases of gall stone. I had the misgiving that I was in the presence of an unfamiliar affection and was prepared for a surprise when I opened the abdomen; and yet acute pancreatitis did not occur to me, my conception of the clinical picture was so different. But I shall not soon forget this case; the excruciating pain in the epigastrium and the cyanosis; altogether, a clinical picture different from anything that I could recall. To save my colleagues and students the humiliation of making the same mistake, I have thought that it might be well to represent graphically the only sign which this obscure case presented, the white print of fingertips in a slightly cyanosed field just over the site of greatest pain. Attacks of acute hemorrhagic pancreatitis, mild and severe, are probably much more common than is generally supposed, and I am sure that the clinical picture is sufficiently definite to be easily recognized by the general practitioner.

The autopsy was most carefully made by Dr. Opie, whose description of it will follow. The stone, which I could not find in my hurried search at the operation, was almost too minute to have been detected under the circumstances, and even at the autopsy it was only after prolonged handling and probing of the papilla itself outside of the body that the presence of a stone was determined. Opie has found that gall stones have been present in the majority of the more recently reported cases of acute hemorrhagic pancreatitis. In some instances they were, undoubtedly, not carefully searched for, in a few they may have been overlooked and in others they may have passed the papilla, having been arrested in the diverticulum long enough to produce the lesion in the pancreas. If it is true, as this case and Opie's experiments recorded below prove almost beyond question, that acute hemorrhagic pancreatitis may be caused by bile retrojected into the pancreatic duct, the inference that milder lesions and subacute and chronic changes may be produced in the pancreas by the mere presence of bile in its ducts is natural. The fact that the entire pancreas is not always or even usually involved, normal areas being found here and there among the hemorrhagic ones, makes it seem not unlikely that quite small patches may at times be affected and that the symptoms after very limited involvement might be overlooked or misinterpreted. Epigastric pain, rapid pulse, nausea, vomiting and possibly hematemesis coming on either soon or long after operations upon the common duct might in some instances be attributable to lesions in the pancreas.

The Mechanism.—The arrangement of the parts concerned

in the production of acute hemorrhagic pancreatitis reminds me of the hydraulic ram in its primitive form. The ductus choledochus is the feed pipe, the pancreatic duct the delivery pipe and the calculus the ball valve or stop cock. Although I know of no experiment to determine the force with which bile may be ejected from the gall bladder, it is conceivable that the sudden and complete interruption of the flow of bile during digestion by a calculus might give rise to a retrojection spurt of considerable volume and velocity. But whether this force is considerable or not, since the pancreatic juice and the bile are secreted at almost the same, quite low (20² mm. of water) pressure, it would probably be sufficient, as Dr. Opie will show, to drive the bile into the pancreatic duct under the proper conditions.

Why is pancreatitis hemorrhagica acuta such a rare disease?

1. That bile may be retrojected into the pancreatic duct, the stone must be (a) too small to occlude the pancreatic duct or interfere with the force of the jet and at the same time (b) too large to pass the papilla.

2. A narrow papillary orifice, such as we found in my case (a rare condition), would predispose to this affection, because many stones small enough to fulfill (a) the first condition are too small to fulfill (b) the second.

3. One calculus would be more likely to cause the pancreatitis than several, for other stones in this duct, unless very small, would weaken the force of the bile-spurt which drives the ball valve against the papillary orifice. I have elsewhere called attention to this fact.¹

4. The gall bladder must perhaps be normal or nearly so; not thickened, shrunken or weakened by inflammation. Accordingly, one must have a calculus or calculi which have produced insignificant changes, if any, in the walls of the bladder.

5. The anomalies which Dr. Opie will consider protect a certain proportion of cases.

6. A predisposition may be necessary, as is given by adiposis and excessive use of alcohol.

Apropos of what I have said as to the possibility of mild attacks of hemorrhagic pancreatitis after gall stone operations, Dr. Finney has just told me the story of a most interesting and perhaps not wholly unique case. Four months ago he did a choledochotomy for 2 large soft stones in the common duct. The duct was enormously dilated, the gall bladder atrophied. The stones were almost as mushy as damp salt, and crumbled to pieces in the duct. The detritus was removed with extreme care and the duct afterwards repeatedly flushed with the physiological solution; notwithstanding this it seemed to Dr. Finney that some grains still remained in the duct. The incision into the common duct was sutured and the convalescence was entirely uneventful except for a trivial leakage of bile beginning about the 7th day p. o. A few days ago, when in robust health, the patient was seized with excruciating pains in the

epigastrium, unlike any that he had ever experienced. Dr. Finney was telegraphed for promptly and reaching the patient in a few hours found him vomiting, collapsed, cyanosed and suffering pain so severe that morphia in large doses did not control it; the pulse was about 160, pressure over the pancreas was unendurable, the abdomen was distended. Acute pancreatitis was suspected, and operation, considering the collapsed condition of the patient, deemed inadvisable. The following day the patient was brought to the Johns Hopkins Hospital, his condition was greatly improved and 48 hours later he seemed perfectly well.

Is it not probable that in this case one of the fragments increased in size may have been responsible for the attack? Was the fragment passed? What were the lesions in this attack? Acute pancreatitis just beginning to be understood will probably soon become a household word.

Treatment.—We must learn to make the diagnosis promptly, and to distinguish gall stone attacks *per se* from those attended with pancreatic complications.

To search for and remove the stone in the diverticulum as soon as possible after the appearance of the first symptoms would be the correct procedure in some cases if the true nature of the attack could be recognized early enough. If this patient of mine had been operated upon and the stone removed at some time prior to the onset of his severe symptoms, perhaps at any time within the first seven or eight days of his illness, it seems probable that his life could have been saved. Without operation there was little if any hope for him, for the conditions responsible for the lesions would have persisted. It was evident at the operation that the common duct was obstructed but the patient's condition absolutely contraindicated prolonged search for the cause, which probably could only have been determined by opening the common duct or the duodenum, so minute was the calculus. Operation should not be undertaken upon cases in collapse, but the bloody fluid, probably highly toxic,² may be hastily evacuated by laparotomy (local anæsthesia) in cases too ill for radical operation.

Of 25 cases of acute hemorrhagic pancreatitis operated upon only two have recovered, a case operated upon by me eleven years ago³ and Hahn's case recently reported.⁴

In his recent article Prof. Hahn expresses a desire to learn if the operation performed by me in the case which recovered was prolonged by the usual search for some cause of intestinal obstruction, and the hope that, in future, inoculations of culture media will be made from the blood-stained abdominal fluid. It gives me pleasure to be able to reply and to state that fat necrosis was at once observed, the diagnosis promptly made and the operation, therefore, probably a short one: drainage was not employed. This patient is alive and apparently well. In the second case, inocula-

² Hahn. Deutsche Zeitschr. f. Chir. Bd. 85. Heft 1.

³ Körte. Die Chirurgischen Krankheiten und die Verletzungen des Pankreas.

⁴ Hahn, l. c.

¹ Halsted. Contributions to the Surgery of the Bile Passages. The Johns Hopkins Hospital Bulletin, January, 1900.

tions from the bloody abdominal fluid were made, and with negative results.

It seems not improbable that, as Hahn states, the rapid evacuation of the bloody fluid in the abdominal cavity may in some cases be beneficial. Hahn believes that this fluid is highly toxic and perhaps infectious, and emphasizes the fact, exemplified by one of the cases which he reports, that large retroperitoneal extravasations of blood cause incomparably less disturbance than we see in these cases of hemorrhagic pancreatitis in which the loss of blood is insignificant. I had read Hahn's article only a few days prior to the operation upon this case and was acting upon his suggestion, but coming so quickly upon the dilated common duct I felt myself compelled to make a hurried search for the cause of the obstruction. I have little doubt that my operation hastened the death of the patient.

If a stone in Vater's diverticulum was the cause of the pancreatitis in my first case, the one that recovered after operation, we must conclude that it passed the papilla, probably during the attack, for it had produced no symptoms from the time of the operation, May, 1890, until June, 1895, when he was examined in the hospital by Dr. Bloodgood. I find that I misinformed Dr. Körte⁵ when I wrote him that my recovered case had had a subsequent attack. The attack referred to occurred in another case, one of suppurative pancreatitis, operated upon and cured by my associate, Dr. Finney.

⁵ Körte; Die Chirurgischen Krankheiten und die Verletzungen des Pankreas. Deutsche Chir. 1898, p. 171.

THE ETIOLOGY OF ACUTE HEMORRHAGIC PANCREATITIS.

BY EUGENE L. OPIE, M. D.

Instructor in Pathology, Johns Hopkins University.

(From the Pathological Laboratory of the Johns Hopkins University and Hospital.)

PATHOLOGICAL REPORT.

In many reported cases of hemorrhagic and of gangrenous pancreatitis symptoms of cholelithiasis have been associated with the fatal illness and at autopsy calculi have been found in the gall bladder or in the bile passages. In a recent article¹ I collected from the literature thirty-one cases of this character and described an additional instance. In eight of these cases, including the one which I reported, a gall stone was found at autopsy lodged near the orifice of the common bile duct or there was evidence that one had shortly before death occupied this position. Since the common bile duct and the duct of Wirsung unite to form the diverticulum of Vater before they enter the intestine, a calculus so located might occlude both ducts. In the greater number of these collected cases though calculi were found at autopsy, none

were situated near the junction of the two ducts. Nevertheless since, as was pointed out, death with intense hemorrhagic inflammation of the gland has in several instances followed within forty-eight hours the onset of symptoms and a calculus has been found near the duodenal orifice of the common duct, it is readily conceivable that a stone temporarily lodged in the position indicated might produce grave alteration of the gland before its final expulsion into the duodenum. In seven of the thirty-one cases death followed the onset of symptoms, intense abdominal pain, vomiting and profound collapse, within forty-eight hours, and at autopsy the pancreas was the seat of hemorrhagic infiltration. In seventeen instances in which the fatal illness was of longer duration, seven days to four months, the pancreas was gangrenous and there was often evidence of previous hemorrhage. There can be little doubt that gangrenous pancreatitis is a late stage of the hemorrhagic lesion.

That acute pancreatic disease is frequently associated with cholelithiasis has been confirmed by cases reported since the preparation of the article referred to. The two conditions were present in three cases recently described by Lund,² in two by Bryant³ and in one by Stockton and Williams,⁴ by Struppler⁵ and by Hahn.⁶ The relative frequency with which acute pancreatitis is accompanied by cholelithiasis is difficult to estimate. In some cases the lesion has been diagnosed upon the operating table and, no autopsy being obtained, the condition of the bile passages has not been determined. In a very large proportion of the cases the autopsy report is so meagre that the presence or absence of gall stones is not evident. Lund records the relatively large number of six cases of acute pancreatitis, one suppurative, five hemorrhagic or hemorrhagic and gangrenous. Two of the five cases he describes as hemorrhagic peripancreatitis. In three of these five cases the gall bladder or the bile passages contained small calculi in large number, while in the remaining two no autopsy was obtained. In the two cases reported by Bryant hemorrhagic pancreatitis was associated with gall stones. In only one of the five cases of Hahn were gall stones present, but in one of his cases hemorrhagic infiltration of the gland followed a pistol shot wound and in another recovery followed operation. Gall stones were, therefore, present in six of eight cases with autopsy described by three writers who have recently reported more than one instance of the disease.

In view of the fact that in several instances a calculus has been found at autopsy so lodged as to occlude the pancreatic duct, there can be no doubt that the frequent association of the two conditions is the result of an etiological relationship. The common bile duct and the larger pancreatic duct lie side by side as they penetrate the wall of the duodenum and are often separated near their junction only by a thin mem-

² Lund. Boston Med. and Surg. Jour., 1900, cxliii, p. 543.

³ Bryant. Lancet, 1900, ii, p. 1341.

⁴ Stockton and Williams. Philadelphia Med. Jour., 1900, vi, p. 649.

⁵ Struppler. Deutsche Arch. f. klin. Med., 1900, lxi, p. 206.

⁶ Hahn. Deutsche Zeitschr. f. Chir., 1900, lviii, p. 1.

¹ Opie. Amer. Jour. of the Med. Sciences, 1901, cxxi, p. 27.

branous septum, while before entering the duodenum at the summit of the bile papilla they unite to form a short channel, the diverticulum of Vater. From a study of the case previously reported it seemed not improbable that a calculus lodged in the common bile duct near its termination might cause partial occlusion of the pancreatic duct and subsequent changes in the pancreas as the result, possibly, of bacterial invasion. This case, as well as those recorded in the literature, afforded, however, no explanation of the pathogenesis of hemorrhagic inflammation. The autopsy recently performed upon the case described by Dr. Halsted has demonstrated a mechanism by which this lesion is produced.

Autopsy.—The body, which is still warm, is that of a large man with very abundant subcutaneous fat. The skin has a bluish cyanotic appearance. Passing downward from the right costal margin to a point 10 cm. from the symphysis pubis is a longitudinal incision, closed in great part by subcutaneous silver wire sutures. Crossing the epigastric region and meeting the first at right angles is a second incision. At their angle of junction the wound is unclosed for a short distance and gauze packed about by rubber protective passes into the abdominal cavity.

The peritoneal cavity contains a moderate excess of blood-stained serous fluid. The general peritoneal surface is smooth. Fat is present in very great amount in the omentum, in front of the peritoneum of the anterior abdominal wall below the umbilicus, in the mesentery, in the retroperitoneal tissue and as appendices epiploicæ upon the surface of the large intestine. Studding the fat in the various situations named and conspicuous upon its translucent surface are small usually round opaque white areas 2 to 3 mm. in diameter, often surrounded by a narrow zone of injection. They are superficially situated and extend usually less than 1 mm. below the surface. They are most abundant in the omentum and in the retroperitoneal fat adjacent to the pancreas. The gauze drain previously mentioned passes between the stomach and the transverse colon and lies in contact with the retroperitoneal fat immediately below the head of the pancreas. Here the tissue has a reddish-black discoloration.

The pancreas is represented by a blackish swollen mass extending from the descending part of the duodenum to the spleen. The fat in contact with its splenic end has a similar blackish color and is soft and friable. The pancreas is greatly increased in size, is irregularly cylindrical in shape and measures 5.2 cm. antero-posteriorly, 5.5 cm. from above down, and 16 cm. in length. The anterior surface is smooth and has an almost uniform black color in places with a reddish tint. On section the gland substance is found to be in great part transformed into black and reddish-black material. The head of the organ for a distance of 2.5 cm. from the duodenum is firm, gray yellow, with well marked lobulation, and has the appearance of the fresh normal pancreas. Tissue which is in immediate contact with this well preserved gland substance is soft and black in color, mottled here and there with small areas of dull red; gland lobulation is still very

obscurely marked. The distal half of the organ shows a similar mottling of black and reddish areas with in places small islands of yellowish, relatively preserved tissue. The largest of these, which is of reddish-yellow color, gradually passing into the surrounding reddish-black, is 1.5 cm. in diameter and is situated near the middle of the body. At the splenic extremity is a slightly smaller mass of intact gland substance. On opening the splenic vein where it lies in contact with the pancreas the intima is found to have a mottled yellow, blackish and red appearance, due to changes in the underlying tissue. Occupying a portion of the lumen is a mixed red and yellow thrombus mass, firm in consistence and adherent to the intima.

The duodenum was opened and the common orifice of the bile and pancreatic ducts examined. The papilla is prominent but its orifice is of small size measuring 1 mm. in diameter. The common bile duct which near its termination is completely embedded in the substance of the pancreas is slightly distended. By very firm pressure on the gall bladder several drops of bile can be squeezed with difficulty into the duodenum. The gall bladder when opened is found to contain a moderate amount of viscid blackish bile; no concretions are present. The termination of the pancreatic duct, which is surrounded by the well preserved pancreatic substance in contact with the duodenum, was exposed by dissection and found to unite with the common bile duct 10 mm. from the summit of the bile papilla. A probe passed down the common duct was stopped 4 mm. from the latter point, and it was not possible to touch it with a second probe passed into the narrow orifice. Careful examination disclosed a small gray-white, very firm concretion 3 mm. in diameter, snugly filling the diverticulum of Vater from which it could not escape through the narrow duodenal orifice. The pancreatic duct, where it passes through the intact tissue of the head, is like the common duct stained bright green with bile.

The heart and lungs are apparently normal. The liver weighs 1350 grms. The surface is smooth and of yellowish color; upon the upper surface of the right lobe are conspicuous slightly depressed dull red areas which are irregular in shape, the larger about 2.5 cm. across. The cut surface of the organ has a bright yellow color, the periphery of the lobules being golden-yellow, the central part reddish. Corresponding to the superficial red areas the liver substance has a similar dull red appearance, the periphery of the lobules being marked by narrow yellow zones. Such altered tissue has at times an irregularly wedge-shaped outline and within it are found portal veins distended and plugged with red thrombus material. Following the vein in one of these areas toward the main portal trunk, the thrombus stops abruptly and near its end is of yellowish-white color, representing probably embolic material from the thrombosed splenic vein. The spleen is not enlarged and weighs 140 grms. The organ is flaccid but fairly firm in consistence.

The stomach contains a small amount of blackish semi-fluid material. The duodenum and remainder of the small intestine contain similar material. The kidneys, weighing

together 290 grms., appear to be normal, except for the presence of opaque yellow striations near the apices of the pyramids. The adrenals, the bladder, the seminal vesicles and the prostate are normal. Upon the intima of the aorta are a few slightly raised opaque yellow patches of small size. The urine contained in the bladder does not reduce Fehling's solution.

Microscopic examination of the pancreas.—A section passing through the line of demarcation between the intact parenchyma in the head of the gland and the adjacent necrotic tissue shows a very abrupt transition from the one to the other. On the one side the pancreatic tissue is well preserved, the secreting cells are normal in appearance and their basal zone stains deeply with hæmatoxylin, while islands of Langerhans are fairly abundant and appear to be normal. The loose interlobular areolar tissue is everywhere infiltrated with red-blood corpuscles; polynuclear leucocytes are present in large number and often form collections of considerable extent. Eosinophilic leucocytes are numerous and fibrin is abundant. Between the acini are a few polynuclear leucocytes. Within the margin of the intact tissue are several small areas where the parenchyma is undergoing necrosis. The secreting cells no longer stain with hæmatoxylin, but assume a homogeneous clear pink color with eosin; the nuclei which are still preserved are much smaller than those of the normal cells and unlike the latter are irregular and distorted and stain homogeneously. Small hemorrhages have taken place into the interacinar tissue of such an area, and polynuclear leucocytes are present in moderate number. Nearby in similarly localized areas the process is more advanced and the parenchymatous cells are replaced by formless material which staining faintly is mingled with a few nuclear fragments and is densely infiltrated with polynuclear leucocytes and red-blood corpuscles.

The transition from relatively normal parenchyma containing a few islands of necrosis to wholly necrotic tissue is very abrupt and is marked by a zone composed of nuclear fragments, polynuclear leucocytes, red-blood corpuscles and fibrin. That part of the section which corresponds to the black and reddish-black material seen macroscopically is necrotic, nuclei are no longer present and though the architecture of the gland is still obscurely definable both parenchyma and connective tissue stain only with eosin. At intervals in areas of varying extent the tissue has a dark brown discoloration due to the presence of brown pigmented material which appears to be changed blood.

Sections from the body and tail of the organ present the appearance described above. In the intact tissue of the tail well preserved islands of Langerhans are particularly numerous. In a section from the body nuclei still persist immediately about an artery, though the surrounding tissue is universally necrotic. Its endothelial cells are swollen and in places are almost cubical. In the media and adventitia, of which the vasa vasorum are preserved, polynuclear leucocytes are very numerous.

In sections stained by Weigert's method for the demon-

stration of fibrin was noted a histological detail inconspicuous by other methods. Capillary vessels in the living tissue near the margin of necrosis as well as in the immediately adjacent necrotic part have undergone hyaline thrombosis and form conspicuous deep blue, often branched, lines as though injected. Examination with high magnification demonstrates at times a close meshwork of fibrils in these vessels. In sections stained with hæmatoxylin and eosin their contents take a homogeneous bright pinkish-red stain and red-blood corpuscles are no longer seen, as in adjacent capillaries.

In sections stained for bacteria with methylene-blue, with gentian violet, and by Weigert's method, none were discovered.

Bacteriological examination.—Plate cultures in agar-agar were made at autopsy from the heart's blood, peritoneal cavity, pancreas (aërobic and anaërobic on hydrocele agar-agar), gall bladder, liver, spleen, and kidney. They were studied by Mr. V. H. Bassett to whom I am indebted for the following report. Cultures from the heart's blood, spleen, and gall bladder gave negative results. The anaërobic culture from the pancreas showed no growth after an incubation of seventy-two hours. The aërobic agar-agar plate from the pancreas contained at the end of twenty-four hours a single superficial colony of a pigment forming coccus whose cultural characters indicated that it was a contamination from the air. The streptococcus pyogenes and the staphylococcus epidermidis albus were isolated from the peritoneal cavity. The colon bacillus was present in cultures from the liver and kidney.

Anatomical diagnosis.—Cholelithiasis; calculus impacted in the diverticulum of Vater partially filling it and occluding its duodenal orifice. Acute hemorrhagic pancreatitis; disseminated abdominal fat necrosis. Partial thrombosis of the splenic vein; embolism and thrombosis of branches of the portal vein.

The preceding autopsy has disclosed a condition which explains, I believe, the pathogenesis of those cases of acute hemorrhagic and gangrenous pancreatitis which are associated with gall stones. The diverticulum of Vater was 10 mm. in length. Lodged at its apex, blocking its duodenal orifice, was a small calculus only 3 mm. in diameter, but too small to pass the narrow opening. Though it occluded the duodenal orifice of the diverticulum it was so small that the orifices of the common bile duct and pancreatic duct were unobstructed. The two ducts were therefore, converted into a continuous closed channel from which it was not possible for either bile or pancreatic juice to escape.

On dissecting the pancreatic duct where it passed through the unchanged parenchyma in contact with the duodenum it was found, like the bile duct, to be stained bright green with bile. Where, as in this case, the two ducts become a closed channel, the entrance of bile into the pancreas or of pancreatic juice into the bile passages would depend upon the relative pressure in the two ducts. The pressure at which bile and

pancreatic juice are secreted being small, any slight difference that might exist would be overcome by the gall bladder, a muscular organ which at intervals forces bile in considerable quantity along the common duct.

A small calculus only partially filling the ampulla of Vater can convert the two ducts into a continuous channel, while a larger stone might simultaneously obstruct the duodenal orifice of the diverticulum and the orifices of the two ducts which enter it, thus damming back bile and pancreatic juice upon their respective glands. In the present case, as previously mentioned, the diverticulum measured 10 mm. in length, the calculus 3 mm. in diameter. In many cases of hemorrhagic and gangrenous pancreatitis gall stones found in the gall bladder and bile passages at autopsy have been small and are often described as pea-sized. This statement is made in the reports of Day,⁷ Cutler,⁸ Kennan,⁹ Simpson,¹⁰ Chiari¹¹ (two cases), Smith,¹² Ehrlich,¹³ Fraenkel,¹⁴ Körte,¹⁵ Morian,¹⁶ Rolleston,¹⁷ Grawitz,¹⁸ Opie,¹⁹ Bryant²⁰ and Lund²¹ (three cases).

Anatomical peculiarities of the diverticulum of Vater might favor or prevent the conversion of the two ducts into a closed channel. The description of the ampulla given by Sappey,²² Testut,²³ Henle²⁴ and Quain²⁵ does not differ materially. It may be described as a somewhat conical cavity into whose base open the two ducts; the apex situated at the summit of the diverticulum is their common duodenal orifice. Its length varies from 6 to 7 mm. according to Testut, from 7 to 8 mm. according to Sappey. Occasionally the two ducts have no common channel, but open by separate orifices upon the summit of the bile papilla. Claude Bernard²⁶ described a variety of termination which has since been observed. The bile duct is prolonged as far as the mucosa of the duodenum, upon which it opens by a circular orifice. The terminal part of the pancreatic duct embraces the bile duct like a gutter and its orifice has the outline of a crescent. Where the ampulla is very short or the two ducts open separately into the duodenum it is evident that an impacted calculus could not render continuous the lumina of the two ducts.

⁷ Day. Boston Med. and Surg. Jour., 1892, cxxvii, p. 569.

⁸ Cutler. *Ibid.*, 1895, cxxxii, p. 354.

⁹ Kennan. Brit. Med. Jour., 1896, ii, p. 1442.

¹⁰ Simpson. Edinburgh Med. Jour., 1897, ii, p. 245.

¹¹ Chiari. Wiener Med. Wochens., 1876, xxvi, p. 291; *Ibid.*, 1880, xxx, pp. 139, 164.

¹² Smith. Brit. Med. Jour., 1897, ii, p. 468.

¹³ Ehrlich. Beiträge z. klin. Chir., 1898, xx, p. 316.

¹⁴ Fraenkel. Münch. med. Wochens., 1896, xliii, pp. 813, 844.

¹⁵ Körte. Arch. f. klin. Chir., 1894, xlviii, p. 721.

¹⁶ Morian. Münch. med. Wochens., 1899, lxvi, p. 348.

¹⁷ Rolleston. Trans. Path. Soc. of London, 1893, xlv, p. 71.

¹⁸ Grawitz. Münch. med. Wochens., 1899, xlvii, p. 813.

¹⁹ ²⁰ ²¹ *Loc. cit.*

²² Sappey. Traité d'anatomie descriptive. Paris, 1889.

²³ Testut. Traité d'anatomie humaine. Paris, 1894.

²⁴ Henle. Handbuch der Systematischen Anatomie des Menschen. Braunschweig, 1873.

²⁵ Quain. Elements of Anatomy. London, 1896.

²⁶ Quoted by Sappey.

I have recently examined the diverticulum of Vater in a small number of cases available. In three specimens (Nos. 3, 11 and 13) the ducts opened into the intestine by separate orifices. The following figures represent the length of the ampulla in these cases:

No. 1	5 mm.	No. 10	2.5 mm.
" 2	6 "	" 11	0 "
" 3	0 "	" 12	6.5 "
" 4	4 "	" 13	0 "
" 5	5 "	" 14	5.5 "
" 6	7 "	" 15	1.5 "
" 7	10 "	" 16	1 "
" 8	7 "	" 17	11 "
" 9	5.5 "			

No. 6 is from the case previously reported, No. 7 the one described in the present article. The figures are cited to show that the length of the so-called diverticulum varies considerably.

Another anatomical factor of considerable importance is the size of the duodenal orifice of the ampulla. Hyrtl²⁷ states that this opening is narrower than the lumen of the gall duct at any point or is at least less distensible so that gall stones often remain here impacted. In the autopsy described the opening measured only 1 mm. in diameter. In most instances it measured 2 to 2.5 mm.; in specimen No. 9 the diameter was 4 mm.

EXPERIMENTAL STUDY.

Hemorrhagic pancreatitis has been produced experimentally by the injection of a variety of irritating substances into the pancreas, but no attempt has been made to reproduce the lesion by the use of bile.

Thirollox²⁸ injected several drops of deliquescent chloride of zinc into the duct of Wirsung in a dog. Death occurred suddenly after a short interval and the pancreas was represented by what appeared to be a blackish clot. Hlava²⁹ injected artificial gastric juice into the pancreatic duct. This fluid, containing hydrochloric acid in the proportion of 1 to 1000, caused death in three days; the pancreas was hyperæmic and in the fat of the omentum and of the mesentery were numerous foci of necroses. Death on the tenth day followed the injection of 5 cc. of artificial gastric juice with hydrochloric acid 4 to 1000; the pancreas was the seat of hemorrhagic infiltration and the omentum and mesentery contained foci of fat necrosis. He suggests that in human cases hyperacid gastric juice may be forced by antiperistaltic action of the intestine into the pancreatic duct, thus causing the condition. Hlava has produced a hemorrhagic lesion of the gland by injecting cultures of the bacillus coli communis, bacillus laetis aerogenes, and bacillus capsulatus of Friedländer, but thinks that the change is the result of the acid products of these organisms.

²⁷ Hyrtl. Handbuch der Topographischen Anatomie. Vienna, 1882.

²⁸ Thirollox. Quoted by Carnot (see below).

²⁹ Hlava. Quoted by Flexner (see below).

Oser³⁰ records the injection of 4 cc. of $\frac{1}{10}$ normal sulphuric acid solution into the pancreatic duct of a dog. Death followed in twenty hours. In the duodenal part of the gland was a hemorrhagic area the size of a pea where the tissue was destroyed and its structure no longer recognizable. By the injection of the ferment, papaine (0.2 grms. in 30 cc. of water), into the duct of a dog, Carnot³¹ caused the death of the animal in twenty-five hours; the pancreas was everywhere infiltrated with blood but there was no necrosis of fat. Smaller doses did not produce hemorrhagic lesions. The same writer produced hemorrhagic pancreatitis by the injection of the diphtheria toxine into the pancreatic duct of a rabbit. A suspension of the bacillus coli communis (12 cc.) caused a similar lesion fatal in twenty-four hours. Subsequent injections of the same organism caused inflammatory changes without hemorrhage.

More varied and successful experiments have been performed by Dr. Flexner³² in this laboratory. In ten experiments performed upon dogs hydrochloric acid varying in strength in different instances from 0.5 to 2 per cent, and in amount from 3 to 8 cc., was injected into the pancreatic duct. In six instances there resulted hemorrhagic inflammation of the gland, accompanied in five by focal fat necroses. In three of these cases death followed the operation within twenty-four hours; in two the animals were killed. In the remaining experiments purulent or chronic interstitial inflammation resulted. Hemorrhagic lesions were produced in two dogs by the use of nitric acid (4 cc. of a 2 per cent solution and 5 cc. of a 1 per cent solution); in one, by the use of chromic acid (8 cc. of a 1 per cent solution). In a second series of experiments sodium hydroxide solution (2.5 to 5 cc. of solutions varying in strength from 1 per cent to 2 per cent) was employed. Hemorrhagic lesions resulted in three cases and were accompanied by fat necrosis in at least two. Suspensions of bacteria were used in a third series. Hemorrhagic inflammation was caused by the bacillus pyocyaneus and in three experiments by the bacillus diphtheriae but was unaccompanied by definite fat necrosis. In two experiments the lesion followed the injection of 5 cc. of a 2 per cent solution of formalin into the duct and was associated with fat necrosis.

The experiments cited show that a variety of substances injected into the duct of the pancreas cause hemorrhagic inflammation. How far they can be used to explain the pathogenesis of human cases is doubtful. The suggestion of Illava that gastric juice may be driven by antiperistaltic action of the intestine into the ducts is not supported by any evidence. The relation of hemorrhagic pancreatitis to bacterial invasion from the intestine has not been demonstrated. The condition observed in the autopsy described has suggested a mechanism by which an irritating substance can make its way into

the organ. Can the hemorrhagic inflammation observed in human cases and produced in animals by means of various irritants be reproduced by the injection of bile into the pancreatic duct?

In the following experiments the duodenum of dogs was opened for a distance of several centimetres opposite the larger pancreatic duct. The blunt pointed nozzle of a syringe was inserted into the orifice of the duct and bile obtained from the same or from a second dog was injected into the organ. The operations were performed with the usual anti-septic precautions and the duodenal wound was closed by submucous mattress sutures. I desire to express my thanks to Mr. Bassett, Mr. Haskell and Mr. W. Marshall for assistance in the performance of these operations.

Experiment 1.—Into the larger pancreatic duct was injected 5 cc. of bile obtained from a second dog. The animal was killed seven days later. The peritoneal cavity contains a small amount of bloody fluid and the surface is injected. The large and several loops of the small intestine are firmly adherent to the splenic arm of the pancreas, and on separating them are exposed pockets containing very thick viscid fluid of dull red color. The walls of these pockets have in places the opaque white appearance of necrotic fat. The splenic part of the gland and the duodenal part, above the duodenal orifice of the main duct, is firm in consistence and both upon the surface and on section shows a mottling of opaque yellowish-white areas separated by deep hemorrhagic red. Over a considerable area at the junction of the duodenal and splenic parts of the gland the tissue is almost uniformly grayish-yellow and is in places softened and disintegrated. Cultures and coverslips from the peritoneal cavity and from the substance of the pancreas contain no bacteria. Microscopic examination of the splenic and duodenal parts of the gland show that wide areas of parenchyma including entire groups of lobules are necrotic and the secreting cells, which have a homogeneous hyaline appearance and are stained deeply with eosin, contain no nuclei. At the margin of such areas red-blood corpuscles and polynuclear leucocytes are present in great number and fibrin is abundant. In places the bodies of the secreting cells have been converted into formless detritus mingled with red-blood corpuscles and leucocytes. The interstitial tissue may be implicated in the general necrosis but often it has undergone very active proliferation and has in small part replaced the disintegrated acini. Islands of intact parenchyma still persist in places and are surrounded by newly-formed fibrous tissue, containing red-blood corpuscles and polynuclear leucocytes.

Experiment 2.—Bile (5 cc.) from a second dog was injected as before. The animal was killed at the end of five days. Lightly adherent to the part of the pancreas which is in contact with the duodenum are several loops of small intestine. In the omental fat are several opaque white areas of fat necrosis, while near the splenic extremity are several inconspicuous foci of a similar nature. In the duodenal part of the gland in the neighborhood of the orifice of the larger duct for a distance of 3.5 cm., there is extensive hemorrhagic infil-

³⁰ Oser. Die Erkrankungen des Pankreas. Nothnagel's Spec. Path. u. Ther., xviii, ii, p. 286. Vienna, 1898.

³¹ Carnot. Paris Thesis, 1898.

³² Flexner. Contributions to the Science of Medicine, Dedicated to Wm. H. Welch, M. D., p. 743. Baltimore, 1900.

tration separating islands of parenchyma. In places the gland substance is soft and of gray necrotic appearance. The splenic part is firm in consistence and at several points are areas of hemorrhagic infiltration. Microscopic examination of sections from the hemorrhagic duodenal part shows wide areas of necrosis implicating both lobular and interstitial tissue. The parenchymatous cells are hyaline and without nuclei. Copious hemorrhage has taken place into these areas and at the margin of intact tissue polynuclear leucocytes are numerous. Fibrin is abundant in the necrotic interlobular tissue. Where widespread destruction has not occurred there has been active proliferation of interstitial tissue replacing in part destroyed parenchyma and containing numerous red blood corpuscles and polynuclear leucocytes. The remaining acini are often separated by newly-formed interstitial tissue and there is the appearance of advanced chronic inflammation. In the splenic part of the gland foci of necrosis with hemorrhage occur and in small scattered areas there is newly-formed connective tissue.

Experiment 3.—After opening the duodenum 5 cc. of bile obtained from a second dog was injected into the pancreatic duct. Death followed within twenty hours. The peritoneal cavity contains several cubic centimetres of bloody fluid and the peritoneal surface has an irregularly distributed, deep red injection. The entire omentum is studded with conspicuous opaque white areas of fat necrosis, usually round, 1 to 1.5 mm. in diameter, and surrounded by a zone of injection. They are most abundant in the neighborhood of the spleen, where superficially and on section they occupy about one-half the exposed surface. In the mesentery of the duodenum near the pancreas they are numerous, but in the remainder of the mesentery of both large and small intestine they are sparsely scattered. Similar foci are present in the retroperitoneal fat and in the properitoneal fat below the diaphragm. The splenic arm and the upper half of the attached duodenal part of the pancreas are swollen and oedematous in appearance and the lobulations are separated by tissue infiltrated with blood. The cut surface has a mottled dull red and gray color, the interstitial tissue being hemorrhagic, while minute hemorrhages are in places seen within the lobular substance. The left lung is the seat of a mucopurulent bronchitis. A culture made from the peritoneal cavity remained sterile. A short bacillus was grown from the pancreas. Microscopical examination shows that the dull red areas of the pancreas represent foci of necrosis where the parenchymatous cells stain only with eosin and no longer contain nuclei. The blood-vessels here are widely dilated and abundant hemorrhage has frequently taken place. Polynuclear leucocytes are present but are not very numerous. Such an area of necrosis and hemorrhage is at times limited to the central part of a lobule group, while the acini further from the central duct are intact. The interstitial tissue particularly of the duodenal part of the gland has an oedematous appearance and contains red blood corpuscles, polynuclear leucocytes and fibrin.

Experiment 4.—By means of a sharp pointed needle 3 cc.

of bile was withdrawn from the gall bladder and injected into the larger pancreatic duct. The animal was killed at the end of seven days. Upon the surface of the pancreas where it is in contact with the duodenum are a few sparsely scattered opaque white areas of small size. In the omentum near the gland are a few similar foci of necrosis. The pancreas is normal in consistence and no change is noted macroscopically. Microscopic examination shows the interstitial tissue of the splenic and duodenal parts of the gland moderately infiltrated in places with blood corpuscles, while here and there it is distended and has an oedematous appearance. The parenchyma is normal in the sections examined.

Experiment 5.—The operation previously described was repeated and 2.5 cc. of bile was withdrawn from the gall bladder and after opening the duodenum injected into the larger pancreatic duct. The dog was killed at the end of four days. The pancreas which is not adherent to the adjacent structures is firm in consistence and has throughout a reddish-gray color, but is nowhere hemorrhagic. On the surface of the duodenal part in contact with the duodenum are sparsely scattered opaque white areas of fat necrosis. Microscopic examination of a section from the duodenal part of the gland shows that newly-formed cellular connective tissue has in a small area replaced the glandular elements. Proliferation of cells has occurred in the adjacent interlobular tissue which contains in abundance red blood corpuscles, polynuclear leucocytes and fibrin.

Should bile enter the pancreas after occlusion of the distal end of the diverticulum of Vater, its only opportunity for escape would be by way of the lesser pancreatic duct. In order to reproduce this condition, in the following experiments the duodenum was not opened, but the duct was exposed where it approaches the intestine, ligated close to the duodenum and partially cut across. By means of a syringe with a blunt nozzle, bile was injected into the distal end of the duct which was then ligated.

Experiment 6.—Into the larger duct was injected 5 cc. of bile obtained by puncture from the dog's gall bladder. The animal died twenty-four hours later. The peritoneal cavity contains no excess of fluid. Opaque white areas of fat necrosis are numerous upon the surface of the duodenal part of the pancreas and in the immediately adjacent fat of the duodenal mesentery. Similar foci are present in both layers of the mesentery near the stomach and pancreas and in the fat in contact with the splenic part of the gland. The interstitial tissue of the duodenal part over an area near the orifice of the larger duct, 2.5 cm. in width, shows deep red hemorrhagic infiltration. The parenchyma throughout the gland is mottled, small dull red areas alternating with more normal gray yellow gland substance. This hemorrhagic appearance of the parenchyma is most marked in the duodenal part of the gland where there are homogeneous dull red areas of considerable extent. Both lungs contain extensive deep red areas which are fairly firm in consistence and exude very abundant frothy serum. Microscopic examination of all parts

of the pancreas shows the presence of numerous foci of necrosis. The gland cells have assumed a hyaline appearance and have lost their nuclei. The blood vessels in these areas are widely distended and at times there is abundant extravasation of red blood corpuscles. Polynuclear leucocytes in moderate number are seen between the necrotic cells. The interlobular tissue is in many places much distended, containing red blood corpuscles, polynuclear leucocytes and fibrin.

Experiment 7.—The operation already described was repeated and 3.7 cc. of bile obtained from the gall bladder of the same dog was injected into the larger duct. The animal was killed three days later. Upon the surface of that part of the pancreas which is in contact with the duodenum and in the fat immediately adjacent to the splenic part are a few opaque areas of necrosis. The pancreas is very firm throughout. On section the glandular lobules are found to be separated by septa of interstitial tissue which are firmer and thicker than usual and near the termination of the larger duct infiltrated with blood. In the duodenal and splenic parts of the gland microscopic examination demonstrates within the lobular tissue numerous small areas where newly-formed, very cellular interstitial tissue replaces groups of acini. The interlobular tissue is infiltrated with red blood corpuscles and often contains in great abundance polynuclear leucocytes and fibrin.

SYNOPSIS OF EXPERIMENTS.

I.—DUODENUM OPENED AND DUCT INJECTED.

Amount of bile.	Mode of death.	Pancreas.	Fat.
No. 1....5cc.	Killed in 7 days.	Hemorrhagic inflammation and sclerosis.	Fat necrosis near pancreas.
No. 2....5cc.	Killed in 5 days.	Hemorrhagic inflammation and sclerosis.	Fat necrosis.
No. 3....5cc.	Died in 20 hours.	Hemorrhagic inflammation.	Extensive fat necrosis.
No. 4....3cc.	Killed in 7 days.	Slight hemorrhagic infiltration.	Slight fat necrosis.
No. 5....2.5cc.	Killed in 4 days.	Slight hemorrhagic infiltration and sclerosis.	Slight fat necrosis.

II.—DUCT OPENED, INJECTED AND LIGATED.

No. 6....5cc.	Died in 24 hours.	Hemorrhagic inflammation.	Fat necrosis.
No. 7....3.7cc.	Killed in 3 days.	Hemorrhagic inflammation and sclerosis.	Slight fat necrosis.

The injection of 5 cc. of bile into the pancreatic duct caused hemorrhagic inflammation of the gland in four dogs, two of which died within twenty-four hours after the operation. Death did not follow the use of smaller amounts and the changes produced in the organ were less wide spread and severe. In every case necrosis of the adjacent fat accompanied the lesion of the pancreas, and in the two instances in which death occurred spontaneously foci of necrosis were abundant and disseminated. In Experiment No. 1, though the entire splenic arm of the gland was the seat of an intense inflammatory reaction, coverslips and cultures demonstrated the absence of bacteria. The presence of bacteria in the pancreas of dog No. 2, which died twenty hours after the

operation, is not surprising since the injection was made through the duodenal orifice of the duct.

Microscopic examination confirmed the diagnosis of hemorrhagic pancreatitis and demonstrated the identity of the experimental lesions with that which occurs in human cases. The injected bile first causes necrosis of the parenchymatous cells with which it comes into contact. They lose their nuclei and their protoplasm assumes a homogeneous hyaline appearance and stains deeply with eosin. The injurious action of the irritant upon the blood-vessels is manifested by the occurrence of hemorrhage into these necrotic areas. An inflammatory reaction now ensues and is characterized by the accumulation of polynuclear leucocytes and fibrin in the interstitial tissue and in the necrotic parenchyma. The necrotic material undergoes disintegration and a rapid new growth of interstitial fibrous tissue in part or wholly replaces it. Where death does not rapidly follow the primary effects of the operation opportunity is given for the occurrence of secondary changes in the gland. The experimental lesion is not in all cases so extensive as that recorded in the accompanying autopsy report. In these experiments a single injection of bile is made, while in the human case bile is repeatedly poured into the organ.

CONCLUSIONS.

(1) A small gall stone impacted in the diverticulum of Vater may occlude the common orifice of the bile duct and duct of Wirsung and convert them into a continuous closed channel. Bile enters the pancreas by way of the pancreatic duct and the pancreas becomes the seat of inflammatory changes characterized by necrosis of the parenchymatous cells, hemorrhage and the accumulation of inflammatory products. Anatomical peculiarities of the diverticulum of Vater do not permit this sequence of events in all individuals.

(2) Injection of bile into the pancreatic duct of dogs causes a necrotizing hemorrhagic inflammation of the pancreas resembling the human lesion, and like it accompanied by fat necrosis. Necrosis of the parenchymatous cells and hemorrhage represent the primary action of the bile; an inflammatory reaction rapidly follows.

(3) The frequent association of cholelithiasis with hemorrhagic and gangrenous pancreatitis is the result of impaction of gall stones at the orifice of the diverticulum of Vater and penetration of bile into the pancreas.

THE JOHN W. GARRETT INTERNATIONAL FELLOWSHIP.

It is gratifying to be able to announce that the John W. Garrett International Fellowship has been founded by William Johnston in connection with University College, Liverpool, in memory of the late John W. Garrett, of Baltimore, and former Trustee of this Hospital, with the title of the "John W. Garrett International Fellowship in Pathology and Physiology."

The Fellowship is to be open to members of Universities and Medical Schools in the United States, without, however, precluding the conferring of the Fellowship upon members of other foreign schools.

The Fellow is to be elected by the Faculty of University College, Liverpool, on the nomination of the Professors of Pathology and Physiology. He is elected for one year, but may be reappointed. He is required to devote himself to research in physiology or pathology and bacteriology, under the direction of the Professors of Physiology and Pathology. The work is to be done in the Thompson Yates Laboratories of University College, but by special permission from the Faculty the Fellow may pursue necessary investigations elsewhere. The expenses of all researches are to be met out of the funds of the laboratory.

NOTES ON NEW BOOKS.

Lehrbuch der Anatomie der Haustiere mit besonderer Berücksichtigung des Pferdes. An Stelle des in 1. und 2. von Leyh, in 3. und 4. von Franck, in 5. Auflage von Martin Herausgegebenen Handbuchs der Anatomie der Haustiere. Vollständig neu Bearbeitet. Von DR. PAUL MARTIN, professor an der Tierarzneischule in Zürich. (Stuttgart: Verlag von Schickhardt & Ebner (Konrad Wittwer), 1901.) Price 40 Marks.

It is a pleasure for those interested in this subject to go through the new edition of the Leyh-Franck Anatomy, thoroughly revised, in fact rewritten, by Professor Martin. The scope of the work is so extensive and the treatment so compact, thorough and scientific that students of veterinary medicine (or any medical students) must rise far above the average in ability and in training to pursue this anatomy.

The work is divided into two large volumes, the first of which is devoted to general anatomy and embryology to the extent they underlie the systems of the body. Then the histology and microscopic anatomy of the organs follow. This arrangement of the general part makes it possible to consider phylogeny with ontogeny without causing confusion. In fact this is necessary. By this arrangement the first volume serves as a broad scientific basis for the second, thus giving a firm foundation upon which the systematic anatomy is easily united with the other morphological sciences.

The author includes with the discussion of the organs their histology and microscopic anatomy, for his experience as a teacher is that such treatment has always been welcomed by his students. In this direction the text is extensive enough and the illustrations sufficiently numerous to serve as a good foundation for these subdivisions of the main subjects.

The second volume is devoted to descriptive systematic anatomy. It is arranged to guide the student in the study of dissections.

All in all the work reminds one somewhat of Quain's Anatomy, or rather of Rauber's revision of it. The illustrations are numerous and excellent, the text is well written and clear, showing that the author is master of the subject.

That an Anatomy of this rank is in its sixth edition speaks much for veterinary education in Europe. Students with a training in anatomy sufficiently broad to grasp this work are raised far above the average veterinarian of America. Fortunately, we have two or three veterinary colleges in which the course in anatomy is up to the level of Martin, and we cordially

recommend this book to them as well as to all others who are interested in the comparative anatomy of the domestic animals.

A Text-Book of Histology. By A. A. BÖHM and N. VON DAVIDOFF. Edited by G. CARL HUBER; translated by H. H. CUSHING. (Philadelphia: W. B. Saunders & Co., 1900.)

It is a matter for congratulation that so good a book as Böhm and von Davidoff's Histology has been translated into English, and put within the reach of all American students of anatomy. It would seem at first sight that a book of this character written in German could be as easily and widely used as an English edition; but such is by no means the case. To the average student a foreign language forms a very considerable obstacle, and a good book written in German, for example, is not infrequently put aside for a less valuable English substitute. In editing an English version of what is one of the best short Histologies in any language, Dr. Huber has rendered a valuable service to both teachers and students; and in bringing this book to a certain extent up to date, he has made it a most valuable laboratory guide.

It is somewhat to be regretted that the editor did not in this work bring all the parts of the book equally in touch with the latest literature. Many of the descriptions seem to have been left as they were in the original, no regard being given to work which has been done since that edition was published. Some organs, on the other hand, are described in great detail, and fairly full references made to the original sources of information. An excellent account is given of the epithelial and connective tissues, and the addition of Dr. Huber's own work to the section on nervous tissues makes it an interesting and valuable article. The chapters on muscle and blood, however, might with advantage be much amplified. The lymph and thyroid glands also merit more attention than they receive. Very good descriptions are given of all the thoracic and abdominal viscera, especial attention being given in almost every case to the nerve supply. This influence of Huber's own work is felt in many of the chapters, and the detailed description of nerve endings in the various organs is a conspicuous feature of this edition of the book. The blood supply in most cases is much less fully described.

The illustrations are excellent throughout, and good judgment is shown in their selection. There are very few that could be omitted with advantage. Perhaps the same criticism, however, could be made of the figures as has been suggested concerning the text. Some chapters are excellently illustrated and others only indifferently so. This is hardly to be avoided in treating so large a subject in such a brief space.

The part which deals with special technique is one of the most valuable in the book. It is compiled with the greatest care and contains numerous methods which will be of very real assistance to laboratory workers. The methods of maceration and digestion of tissues will be found especially instructive in laboratory courses.

A good index and a list of the articles referred to in the text complete this excellent book, upon the appearance of which Dr. Huber is to be sincerely congratulated. It is without doubt one of the best brief text-books of Histology to be obtained at present.

J. B. MACCALLUM.

Hand Atlas of Human Anatomy. By WERNER SPALTEHOLZ, Extraordinary Professor of Anatomy in the University and Custodian of the Anatomical Museum at Leipzig, with the advice of WILHELM HISS, Professor of Anatomy in the University of Leipzig. Translated from the third German edition by LEWELLYS F. BARKER, Professor of Anatomy in the University of Chicago, with a preface by FRANKLIN P. MALL,

Professor of Anatomy in the Johns Hopkins University at Baltimore. Vol. 1, Bones, Joints, Ligaments. Cloth, \$3.50. Pages 235, figures 1-280. (*Leipzig: S. Hirzel; New York: G. Stechert.*)

Descriptive anatomy is essentially a study of form and of spacial relations. Pictures and models constitute the most satisfactory means of expressing these phenomena. Illustration is therefore a most important factor in anatomical study. Pictures showing the main anatomical conditions which the researches of centuries have revealed serve as the best guide in dissection; pictorial illustration is the best means of recording the work of this kind. The student should have good pictures to aid him in his task. He should sketch the results of his dissections in order to formulate clearly the ideas revealed to him by the work.

Anatomical illustration is an interesting subject. Before the beginning of the nineteenth century it was the habit of the anatomist to make a rough sketch of a dissected part. This sketch was then turned over to the engraver, who elaborated the drawing on wood or copper, eliminated its crudities and produced a fine picture. The effect of the engraver's imagination is most clearly seen perhaps in the plates that accompany the work of Versalius and the earlier anatomists. The eviscerated subject of the dissection may there often be seen smiling in the midst of a beautiful landscape. As a rule, parts of the body are shown out of their true positions in the body, often considerably distorted, in order to show the front and back of the same object in the same picture.

In the early part of this century the lithograph was introduced as means of illustration. Here too the hand of the lithographer could be relied upon to correct and elaborate original sketches. Many of the plates made by this process are very beautiful, though here, as in the case of the engraving, there has always been the danger of error owing to the elaboration being made from the drawing, not from the object.

Of recent years the attempt has been made more and more to picture the various parts of the body in their true positions relative to the body contour, to picture the deeper muscles, for instance, as they appear when the superficial muscles have been removed, to show nerves and arteries by representing parts covering them as cut away instead of pulled aside. This has necessitated much more care in the preparation of the parts to be pictured; it has necessitated much more skill on the part of the artist who attempts to depict the parts in their true relations and proportions. Unless the anatomist is an artist of unusual skill and ability he must call in the services of a trained artist if he wishes to illustrate his work well.

This necessity is rendered still more imperative by the modern methods of making plates by the aid of photography. The anatomist cannot hand over a rude sketch to the publisher who desires that the cheaper photograph methods of reproduction be used. The crudities of the sketch appear in the reproduction with startling distinctness. The reproduction appears less well finished instead of better finished than the original. The trained artist who can make drawings that can stand mechanical reproduction has become a necessity. In many ways this is a great gain. It is far better that the elaboration should be made from the object itself, as is the case when an artist is employed, rather than from a sketch, as was the case in the old days of engravings.

Good pictures, moreover, are seldom possible without the aid of a constructive imagination. Anatomical pictures reproduced from photographs of dissections are with few exceptions barbaric in their crudity. Photography alone can be depended upon only when the object pictured is extremely simple or when the very greatest care is taken in making the dissection and the

photograph is afterwards carefully retouched. Rüdinger's beautiful Nerve Atlas shows with what success this may be done.

In the Atlas before us modern conventional methods of illustration have been used, but they have been used with a perfection not hitherto seen in text-books of human anatomy. The drawings have been made by skilled artists and for the most part from careful dissections especially made for the purpose. Wash-drawings reproduced in half-tone are used to illustrate detailed structures and outline drawings are freely used for the purpose of pointing out relations. In illustrating the ligaments the bones are toned yellow for contrast. Colors are also used with effect in the volume on the muscles and blood-vessels which has appeared in German but has not yet been translated into English.

Spalteholz is well acquainted not only with the literature of anatomy but also with practical dissecting. His experience has led him to choose points of view both striking and instructive. Throughout, the attempt has been made to show things in their true relations.

In the volume before us (Vol. 1, Bones, Ligaments and Joints) there is a preface by Prof. Mall in which the value of pictures to the student of anatomy is emphasized, and one by the author in which the general scope of the work is set forth. We could wish that Spalteholz had authorized the translation of his very excellent preface to the German edition. The English of the preface prepared for the translation is far from idiomatic.

The points illustrated in the various pictures are designated by printing their Latin title in full at the margin of each figure.

The bones of the skull are first depicted, several views of each bone being given in order that all the main points may be illustrated. The method of showing the relations of several of the bones is particularly happy. An individual bone, for instance the ethmoid, is drawn carefully in detail. The neighboring bones are drawn in simple outline. Following the illustrations of the individual bones several fine pictures are given of the skull as a whole, and of the chief cavities of the skull; the vertebrae and ribs and the bones of the limbs are then taken up in detail. A very good picture of the skeleton of the thorax is given. On outline drawings muscle attachments are indicated. The section on the ligaments is very satisfactory and is much more extensive than is common in the text-books. The internal architecture of the bones is shown in several special drawings.

Nomenclature is another most important consideration in the study of anatomy. The great wealth of detail which four centuries of earnest work has brought to light concerning the structure of the human body has been accompanied by an even greater mass of names. Investigators who have found nothing new or who have rediscovered facts already known have not hesitated to coin new terms until descriptive anatomy fairly groans under the load of terminology which rests on its shoulders. A great advance was made by the Anatomische Gesellschaft at their meeting in Basel in 1895, when they adopted a list of descriptive terms which tend greatly to simplify the subject (*His: Supplementband zur Anat. Abtheilung des Archiv f. Anatomie u. Physiologie, 1895*).

The "New Nomenclature" has been used systematically throughout the book with a few unimportant exceptions. We believe that it is a mistake, however, to give a Latin name to every nook and corner of the human body. The more definite structures of the human body, like the bones, the main muscles, the larger arteries, veins and nerves and similar structures, are best designated by a specific name. Most of these terms have been derived from the Latin and by usage have become embodied in the various modern languages, sometimes unchanged, sometimes with slight alteration. Thus *clavicle*, *humerus*, *femur*, *biceps*, are all words in more or less common use in English. We think it is a very grave mistake, a relic of unprogressive scholasticism, to make use of Latin when terms are used to

describe as well as designate various definite structures of this nature. In the description of the frontal bone we can see no possible advantage in an English book in writing "In the medial part of the margo supraorbit. there is often a shallow notch, *incisura frontalis* (rarely a *foramen frontale*) (for the a. frontalis; r. frontal. n. frontal.) and lateralward from this a *foramen supraorbitale* or an *incisura supraorbitalis* (for the a. supraorbit.; n. supraorbit.) the anterior convex surface, *facies frontalis*"—etc. This great mass of descriptive Latin terminology merely serves to confuse the student and to take his mind from the essential to the unessential, from the object to the descriptive term. An absurd amount of detailed acquaintance with dissociated parts of the body is at present demanded of the medical student. It is a pity to continue to add a mass of Latin to his burden at the very time that he is beginning to be freed from the shackles of therapeutical botany and its barbarisms.

The main object of an anatomical atlas is to furnish good, clear pictures of the various parts of the body. The text is of minor importance and its chief function is to point out the relations revealed by the pictures and the relations of the pictures to one another. This function is admirably served by the text accompanying the illustrations in Spalteholz's atlas. Such a text confessedly does not take the place of a good text-book. In addition to the atlas the student needs a book in which the dry subject of descriptive anatomy is brightened and enriched by treating of the various parts of the body in their relation to physiological phenomena, to embryology and to comparative anatomy. Gegenbauer's *Anatomie des Menschen* is an admirable example of such a text-book in which the side of embryology and comparative anatomy is especially emphasized.

The English reading student of medicine is fortunate in having had translated for his use this excellent Atlas of Spalteholz. He is especially fortunate in having a translation that has been made by a man of the marked ability of Professor Barker. Professor Barker has been very true to the original text and yet has been able to give us a text exceptionally smooth for a translation so literal.

The printing of the book shows the care and nicety that distinguishes the firm of Hirzel.

We could wish that there were more pictures in this volume in which the skeleton as an organic whole were shown. For instance, not only is there no picture of the skeleton as a whole, but there are none of the limbs as a whole. It is not enough, we think, to give in an atlas merely the hand, the forearm and the humerus as separate parts.

In comparing the illustrations of this Atlas with text-books of a similar scope we find that that of Toldt is the one most similar to it in scope. The beautifully illustrated text-books of Sappey and of Testut are much more expensive and have a different function to perform. Compared with Toldt's Atlas we find the pictures in Spalteholz are more delicate in detail and less diagrammatic. On the other hand, the pictures in Toldt are made sharp and vigorous, owing to the dependence on lines rather than on light and shade. Toldt also has done well in showing the organs in relation to larger areas of the body. The superiority of the pictures in Spalteholz lies in their natural tone.

CHARLES RUSSELL BARDEEN.

BOOKS RECEIVED.

A Practical Treatise on Malaria Medica and Therapeutics. With Especial Reference to the Clinical Application of Drugs. By John V. Shoemaker, M. D., LL. D. Fifth edition, thoroughly revised. (Students' Edition.) 1900. Svo. 766 pages. F. A. Davis Company, Philadelphia, New York, Chicago.

Medical and Surgical Reports of the Boston City Hospital. Eleventh Series. Edited by Herbert L. Burrell, M. D., W. T. Councilman, M. D., and Charles F. Withington, M. D. 1900. Svo. 254 pages. Published by the Trustees, Boston.

American Text-Book of Physiology. Edited by William H. Howell, Ph. D., M. D. Second edition, revised. Volume II. 1901. 4to. 553 pages. W. B. Saunders and Company, Philadelphia and London.

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In the methods of instruction especial emphasis is laid upon practical work in the Laboratories and in the Dispensary and Wards of the Hospital. While the aim of the School is primarily to train practitioners of medicine and surgery, it is recognized that the medical art should rest upon a suitable preliminary education and upon thorough training in the medical sciences. The first two years of the course are devoted mainly to practical work, combined with demonstrations, recitations and, when deemed necessary, lectures, in the Laboratories of Anatomy, Physiology, Physiological Chemistry, Pharmacology and Toxicology, Pathology and Bacteriology. During the last two years the student is given abundant opportunity for the personal study of cases of disease, his time being spent largely in the Hospital Wards and Dispensary and in the Clinical Laboratories. Especially advantageous for thorough clinical training are the arrangements by which the students, divided into groups, engage in practical work in the Dispensary, and throughout the fourth year serve as clinical clerks and surgical dressers in the wards of the Hospital.

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2. Graduates of approved colleges or scientific schools who can furnish evidence: (a) That they have acquaintance with Latin and a good reading knowledge of French and German; (b) That they have such knowledge of physics, chemistry, and biology as is imparted by the regular minor courses given in these subjects in this university.

The phrase "a minor course," as here employed, means a course that requires a year for its completion. In physics, four class-room exercises and three hours a week in the laboratory are required; in chemistry and biology, four class-room exercises and five hours a week in the laboratory in each subject.

3. Those who give evidence by examination that they possess the general education implied by a degree in arts or in science from an approved college or scientific school, and the knowledge of French, German, Latin, physics, chemistry, and biology above indicated.

Applicants for admission will receive blanks to be filled out relating to their previous courses of study. They are required to furnish certificates from officers of the college or scientific schools where they have studied, as to the courses pursued in physics, chemistry and biology. If such certificates are satisfactory, no examination in these subjects will be required from those who possess a degree in arts or science from an approved college or scientific school.

Candidates who have not received a degree in arts or in science from an approved college or scientific school will be required (1) to pass, at the beginning of the session in October, the matriculation examination for admission to the collegiate department of the Johns Hopkins University, (2) then to pass examinations equivalent to those taken by students completing the Chemical-Biological course which leads to the A. B. degree in this University, and (3) to furnish satisfactory certificates that they have had the requisite laboratory training as specified above. It is expected that only in very rare instances will applicants who do not possess a degree in arts or science be able to meet these requirements for admission.

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A CASE OF ARTERIAL DISEASE, POSSIBLY PERIARTERITIS NODOSA.¹

BY FLORENCE R. SABIN, M. D.

Mrs. R. G., æt. 32, was admitted to the Johns Hopkins Hospital on October 21, 1900, in the service of Dr. Osler, to whom I am indebted for the opportunity of reporting the case. She died October 26, 1900. She complained of weakness and stomach trouble. The family history was unimportant. She had been married eleven years, had had three children and no miscarriages. She had had measles and possibly malaria. She was a well, strong woman up to four years previous, when she had an attack of dropsy. For this she was treated at the St. Luke's Hospital, New York City, where the diagnosis of chronic nephritis and endocarditis was made. Since that illness she had never felt well, had had shortness of breath and amenorrhœa. There was no history of syphilis. She had never taken alcohol.

The present illness began in August, 1900, two and a half

months before admission. During the summer she had loss of appetite, indigestion, vomiting and weakness. In August she had attacks of severe shooting pains in the arms and legs. She said that the veins in her arms and legs were swollen and painful to the touch. At the same time she had pain in the epigastric region. On the 19th of September she went to bed with an attack of vomiting which continued four or five days. From that time on, 5 weeks, she had been almost confined to bed. She had had occasional attacks of vomiting, the vomitus being green and containing undigested food but no blood. The bowels had been constipated, the stools light yellow. At the time of admission, she was having diarrhœa with 2 to 4 stools a day. Two weeks before admission her flesh became tender to the touch, and she was unable to move in bed on account of pain. She had lost weight and strength rapidly. Once during the attack she had a rash like measles over the trunk. It lasted four or five days.

¹ Read before the Johns Hopkins Hospital Medical Society, December 17, 1900.

She had had frequency of micturition and occasional swelling of the feet. The urine had been scanty in amount.

On admission she looked extremely ill. There were emaciation, anæmia and asthenia. The skin was sallow, the lips and mucous membranes bloodless, the sclerotics blue. There was a brownish pigmentation of the face, hands and arms. The small muscles of the hands were atrophied. The lungs were negative, the heart not enlarged and its sounds were normal, save for a soft systolic murmur heard best in the pulmonic area. The arteries showed an extreme grade of annular sclerosis. Both radials were calcified so that no pulsation could be felt at the wrist. The pulse was taken at the elbows. The brachials were beaded and could be felt as a series of annular rings. The mammary artery was calcified. The right one could be seen as a string of beads crossing three or four ribs. (Dr. Osler.)

In each popliteal space there was a row of small, hard nodules about the size of a split pea. Two were excised and proved to be made up of lime salts. They were directly under the skin, where the vessels were too small to make out any relations. Scattered over the abdomen were similar nodules; they felt softer and seemed more in the muscle than in the skin. Just above the umbilicus and over both tubera ischii were areas of firm induration in the skin measuring about 4 by 5 cm. Those over the ischia were nodular. She described them as warts.

The abdomen was sunken, the walls so thin that the coils of intestine were plainly seen. There was extreme tenderness in the epigastrium. The liver dulness extended from the 5th rib to a point 3.5 cm. below the costal margin in the mamillary line, and 9.25 cm. below the tip of the ensiform in the median line. The edge of the spleen was palpable 1 cm. below the costal margin. The stomach measured 22.5 by 11 cm. after inflation; it was displaced so that its lower border was 7.5 cm. below the umbilicus. No masses could be made out. Vaginal examination was negative, except that there was one small nodule on the vulva. There were no sears. The cervix and uterus were small and there were no masses in the pelvis. There was a slight purulent discharge in which no gonococci could be found. There was no glandular enlargement. The patellar reflexes were exaggerated.

The blood examination was as follows: On October 22 the fresh specimen showed considerable variation in the size and shape of the red cells, the average diameter being less than normal. The red corpuscles were extremely pale. There was much fibrin and the blood platelets were extraordinarily increased. (Dr. Thomas B. Fletcher.) October 22, hæmoglobin, 22 per cent; red blood corpuscles, 1,772,000; white blood corpuscles, 50,000. The differential count of 312 leucocytes showed: polymorphonuclear leucocytes, 91 per cent; small mononuclear leucocytes, 2 per cent; large mononuclear leucocytes, .9 per cent; transitional leucocytes, 2 per cent; eosinophilic leucocytes, 2 per cent; two normoblasts. October 25, white blood corpuscles, 81,000. October 26, hæmoglobin, 21 per cent; red blood corpuscles, 1,704,000; white blood corpuscles, 116,000.

The fresh specimen was the same as before, the increase in leucocytes being due to the polymorphonuclear forms. The blood examination showed then a secondary anæmia and a pure leucoeytosis.

The temperature was subnormal throughout, the range being 96° to 97.8°. This includes simply the last week of the illness. At the same time the pulse was rapid, ranging between 104 and 124. It fell to 90 on the day of her death. The urine was scanty in amount, 180 cc. being the highest record for the 24 hours. She had, however, from 2 to 4 stools a day. The specific gravity of the urine was 1010; it was almost colorless and had a considerable trace of albumen and a few finely granular and epithelial casts. On October 25 there was almost no urea in a 24-hour mixed specimen. There were but four or five small bubbles of gas generated in the sodium hypobromate solution. Notwithstanding this low excretion of urea the mind was clear; she was drowsy but awakened as soon as any one stepped to her bed, and she was not in coma until four hours before death.

During her stay in the hospital her chief complaint was of pain and burning in the stomach. This was worse on swallowing when she said that she felt a burning like fire all the way down. She had great thirst but little appetite. At times the muscles of the arms and legs were tender to pressure and again the skin over the hips became so sensitive that she would cry out at the slightest touch. Pressure over the epigastrium always made her cry out with pain. Her sleep was disturbed, occasionally waking in fright. On the day of her death there were subcutaneous hæmorrhages on the legs, and the feet and hands became cyanosed and cold. It is a matter of great regret that no section could be obtained. Her people were strict Jews and took her home as she was dying, evidently in dread of an autopsy. When she left the hospital at 5 P. M. her mind was perfectly clear; she was conscious when she reached home but soon fell asleep and died in four hours without waking.

At first the case was considered to be Bright's disease with secondary anæmia but the presence of the nodules suggested the necessity of further study, and it was found that the clinical features of the disease corresponded with the case of periarteritis nodosa, described by Kussmaul and Maier in 1866. A good account of this case was found in Albutt's System of Medicine.

Four cases of periarteritis nodosa have been described. In all of the lists in the literature, a fifth case of multiple aneurisms due to syphilis and reported by Chvostek and Weichselbaum in 1877, is included.

Case I.² In 1866 Kussmaul and Maier described a hitherto unknown arterial disease, which they called periarteritis nodosa, associated with Bright's disease and progressive muscular atrophy. The case was a young tailor, aged 27. His illness lasted a little over a month. He complained of staggering, chilly feelings with fever, and of having his hands go to sleep. They describe him on admission as so sick that

² Kussmaul A. and Maier, R. Deut. Arch. f. klin. Med., 1866, Bd. i, S. 484-518.

the prognosis was made before the diagnosis, that on first sight he was known to be a lost man whose days were few and numbered. This was true of our case. Their case was observed for one month, the entire duration was seven weeks. The symptoms were as follows: pains in the muscles both spontaneous and on pressure, areas of hyperæsthesia of the skin, great weakness which developed rapidly, loss of appetite, pain in the abdomen, especially in the hypochondriac region, and pain in the groins. There was great thirst, at first constipation, later diarrhœa. Sleep was disturbed but the mind was clear throughout. A progressive paralysis developed, beginning with the small muscles of the hands and gradually including the entire body.

The signs were of extreme anæmia, a "chlorotic marasmus." The temperature range was 97.5° - 102.5° F.; it was never high and much of the time there was no fever. In contrast with the low temperature, the pulse was rapid, 112-132. Heart and lungs were normal, liver and spleen not enlarged. There was muscular atrophy beginning with the small muscles of the hands. The urine was diminished in amount, of low specific gravity, 1011-1019, and contained albumen and casts, at first blood also. Three days before death small subcutaneous nodules were felt over the breast and abdomen. These had developed during the course of the disease.

A section was obtained in which the interest centred on these nodules. They were found on the small and medium sized arteries of the muscles and viscera; the heart and lungs, liver, spleen, alimentary canal, kidneys and especially the mesentery showed them, while the arteries of the brain, the aorta and its branches were exempt.

Case II.³ In 1878, Meyer described a case much like Kussmaul and Maier's. It was a man, æt. 27. He was sick 8 weeks, and was under observation most of this time. He complained of pains in the neck, calves of the legs and groins. There was a history of gonorrhœa and syphilis. He showed extraordinary prostration. There were attacks of pain in the stomach and pressure over it was unendurable. The bowels were constipated. There were muscular pains but no paralysis and no disturbance of sensation. The mind was clear but toward the end he became irritable and restless.

The signs were extreme anæmia, a "chlorotic marasmus." The pulse range was 92-108, the temperature reached 104° in the early part of the disease, later the daily range was from 98.8° to 101.8° , and finally it was continuously normal. The heart and lungs were normal, the liver and spleen became enlarged while under observation. The urine was decreased in amount and showed albumen. There was transient œdema of the feet and legs. The nodules were not found before death. On section nodules were found with the same distribution as in Case I. Meyer regarded the nodules as aneurisms.

Case III.⁴ Fletcher's case was a woman, æt. 49. The duration was about 2 months, and she was under observation

at the Freiburg Clinic for the last 3 weeks. There was no history of syphilis; her husband had died of tuberculosis. She was fairly well nourished, and there was a peculiar staring expression of the face. In our case a retraction of the upper eyelids gave a staring expression. There was occasional vomiting and alternating constipation and diarrhœa. She had cough and expectoration. The physical signs of the heart were normal save a modification of the first sound at the apex. There were a few râles at the apices of both lungs. The liver was small, the spleen large. The temperature range was 98.6° to 104° , the pulse 96-138. The urine had a trace of albumen and there was œdema of the feet and legs. No note is made of anæmia nor of a blood examination. The case was thought of before death as either typhoid fever or miliary tuberculosis.

Section showed no tuberculosis. Nodules were found in all the viscera except the brain. The liver and spleen were both enlarged. The autopsy was made by von Kahlden.

In 1894 von Kahlden⁵ saw a second case. It was a woman, æt. 52. The duration 12 weeks, but she was under observation only one day. She complained of fever, loss of appetite and pain in the right hypochondrium. She had had sweating, pain in the arms and legs and great weakness. While under observation she complained of the pain in the stomach as a terrible burning. There was constipation. Sleep was disturbed but the mind was clear. The signs were as follows: the temperature was 99.8° , normal at the end; the pulse was 140. The anæmia was extreme, the skin being light yellow. She had had transient œdema of the face. The physical examination is not given but the section showed no enlargement nor valvular lesion of the heart. The lungs were firm but not airless. The spleen was not enlarged. Nodules were found in the muscles of the chest and tongue and in all the viscera except the brain. They were most numerous in the mesentery.

These four cases were all proved by autopsy; and clinically the case herein reported presents the same features. The lesions of the disease are nodules on the arteries of the muscles and viscera. The symptoms are associated with the muscles, the circulatory system and the alimentary canal. The muscles give pain, occasionally paralysis and atrophy; the circulatory system anæmia accompanied by an asthenia, similar to that in Addison's disease. The pulse rate is rapid, the temperature relatively low. There is fever at first, later normal or subnormal temperature. The chief symptom is gastrointestinal; namely, pain in the stomach accompanied by loss of appetite, thirst, vomiting, constipation and diarrhœa. The signs of Bright's disease are present in the urine but œdema is slight and transient and the mind is clear throughout.

The cases have a wider interest than is due their rarity on account of their pathology. Meyer and Eppinger consider the nodules as aneurisms of the small and medium sized

³ Meyer, P. Arch. f. path. Anat. u. Phys. u. f. klin. Med., 1878, Bd. lxxiv, S. 277-319.

⁴ Fletcher, H. M. Beitr. z. path. Anat. u. z. allg. Path., Jena, 1891, xi, 323-343.

⁵ von Kahlden, C. Beitr. z. path. Anat. u. z. allg. Path., Jena, 1894, xv, 581-601.

arteries. These aneurisms are considered by some to be of syphilitic origin. On the other hand, Chvostek, Weichselbaum, Fletcher and v. Kahlden think that the nodules are inflammatory, or allied to the infectious granulomata and that the aneurisms are secondary to this process. It is a matter of great regret that we could not secure an autopsy in our case; the blood counts showing a pure leucocytosis of a high grade point, it seems to me, toward the inflammatory nature of the disease.

DISCUSSION.

DR. WELCH.—It is interesting that Dr. Osler and Dr. Sabin are willing to make this diagnosis without an autopsy, that is, that they consider the clinical picture sufficiently distinctive, with these nodules, to justify the diagnosis. I judge from the summary of the histories of other cases that there has been considerable uniformity in their characters. The number seems, however, too small for more than tentative conclusions.

TYPHOID INFECTION WITHOUT LESION OF THE INTESTINE. A CASE OF HÆMORRHAGIC TYPHOID FEVER WITH ATYPICAL INTESTINAL LESIONS.¹

BY EUGENE L. OPIE, M. D.,

Instructor in Pathology, Johns Hopkins University,

AND

V. H. BASSETT.

(From the Pathological Laboratory of the Johns Hopkins University and Hospital.)

The intestinal lesions of typhoid fever vary greatly in extent and distribution. Swelling, necrosis and ulceration of the Peyer's patches are usually present throughout a considerable proportion of the lower ileum, but at times a single small ulcer may be the only macroscopic evidence of the intestinal disease. Occasionally the small intestine appears to be entirely unaffected, and hyperplasia and necrosis are confined to the lymphatic apparatus of the large intestine. Doubtless many mild cases run their course without any ulceration of the swollen patches. In a number of cases no intestinal lesions have been found at autopsy, though the clinical history has corresponded to that of typhoid fever and after death the typhoid bacillus has been demonstrated in the organs. To explain such cases one may assume that the organism can enter the body through the intestine without producing any lesion, or that the intestinal tract is not the only path by which it can enter.

The following case, which has directed our attention to this subject, resembles very closely those which have been described as instances of typhoid fever without intestinal lesion:

A. L., female, aged ten years, was admitted to the Johns Hopkins Hospital in the service of Dr. Osler July 14, complaining of pain in the abdomen and weakness. Her family history is unimportant. During the preceding spring she had had measles and has since been slightly deaf but otherwise has had good health. Her present illness began on July 9 with malaise, headache and backache. The bowels moved five or six times and she complained of some pain in the abdomen. On the following day she felt feverish and the diarrhœa and abdominal pain continued. Headache persisted but the diarrhœa became less severe and the pain dis-

appeared. She vomited occasionally. There was no bleeding from the nose.

On admission the child, who was well nourished, appeared drowsy and uncomfortable and complained of some pain in the abdomen. Her mind was clear. The pulse was of small volume, easily compressible and not dicrotic, one hundred to the minute. Examination of the heart and lungs disclosed no abnormality. There was no abdominal distention. A few typical rose-spots were seen upon the abdomen and lower thorax. The spleen was felt at the costal margin when the patient lay on her side and its edge was firm. The temperature on admission was 102.4°. The Widal reaction was obtained on the following day the blood serum diluted 1 to 50, causing agglutination of the typhoid bacillus.

During the first three days after admission the patient complained of much abdominal pain. There was some distention of the abdomen and some tenderness which was most marked in the epigastric region. Beginning on the 6th day in the hospital and persisting a few days pain and tenderness were present in the right hypochondriac region and resistance was here felt. During the first week fresh rose-spots continued to appear. The abdominal pain and tenderness disappeared.

Beginning on the 13th day after her admission to the hospital, bleeding occurred from the lips and nose; at first it seemed as the results of irritation of these parts by continual picking with the fingers. Crusts formed from which blood oozed at times. Over the left cheek below the eye appeared a number of small purpuric areas and ecchymosis occurred into the skin about an excoriation over the right internal condyle of the humerus. The blood, tested by Wright's coagulation tubes, was found to coagulate in four minutes and forty-five seconds. Bleeding from the nose in small amounts

¹ Read before the Johns Hopkins Hospital Medical Society, January 7, 1901.

was persistent. During the night of the 17th day after admission, 60 cc. of bright red blood were passed from the rectum and the following day two soft stools consisted almost entirely of changed blood. The red corpuseles numbered 2,256,000, white corpuseles 3250; the hæmoglobin was 41 per cent.

The note made on the 19th day of observation states that the child seems very ill. The bleeding from the nose has temporarily stopped. The mucous membranes are anæmic. Numerous purpuric areas are scattered over the face, over the posterior surface of the right arm and in small number over the front and back of the trunk.

The stools for four days following the first passage of blood from the rectum contained changed blood in small amounts and there was some abdominal pain but no tenderness nor distention. On the 21st day bleeding from the nose again occurred. The blood examination was as follows: red blood corpuseles 1,768,000, white corpuseles 15,000, hæmoglobin 26 per cent, coagulation time five and a half minutes. There was repeated vomiting of swallowed blood. New purpuric spots had appeared upon the cheeks and shoulders. The patient died with gradually increasing weakness on the 21st day after admission to the hospital, the 26th day of her illness.

During the first few days in the hospital the temperature was almost continuously between 102° and 104°, while subsequently it varied between 99° and 104.5°. The urine contained a trace of albumin and an occasional granular cast.

Autopsy.—The body is that of a well nourished child 128 cm. in length. Over the face are scattered purple ecchymotic spots, the largest 1.5 cm. across. Similar purpuric areas are sparsely distributed upon the trunk, upon the inner surfaces of the arms and upon the legs.

The peritoneum, pleuræ and pericardium are normal in appearance.

The heart weighs 120 gm. Below the epicardium of both ventricles are numerous ecchymoses about 0.5 cm. across. The muscle is pale brown in color and into its substance are a few small hæmorrhages. Below the endocardium of both ventricles but most numerous on the right side are small ecchymotic spots. The valves are normal. The lungs have a grayish-pink surface upon which are scattered areas of deep red color. The tissue is nowhere consolidated.

The liver weighs 820 gm. The tissue has a brownish-red color; the lobulation is well marked. The gall-bladder contains yellow bile. The spleen weighs 180 gm. and measures 11.5 x 7.2 x 4.2 cm. The capsule is smooth. The organ is soft in consistency. The pulp is of a very deep brownish-red color and the Malpighian bodies are well seen.

The stomach contains a small quantity of dark brown fluid material. Its mucosa is thickly studded with small bright red ecchymoses. The duodenum contains a small amount of bright yellow fluid. The jejunum contains brownish, partially clotted and slightly changed blood, and in the ileum, particularly in its lower part, is reddish-brown fluid in which are clotted particles. Passing downward Peyer's patches are

first seen in the lower part of the jejunum and throughout the ileum they are numerous. Their surface is raised but little above the general level and is very slightly nodular; they are conspicuous only because they have remained unchanged while the surrounding mucosa is stained a brownish color by the intestinal contents. Above the ileocecal valve is a very large Peyer's patch 15 cm. in length but otherwise presenting the appearance seen elsewhere. Solitary follicles are visible as small, slightly elevated nodules. The appendix vermiformis is normal. The solitary follicles of the large intestine which are readily seen are often marked by a minute central point of pigmentation.

Lymphatic glands in the mesentery, above the pancreas, and on either side of the aorta, are enlarged, often 1.5 cm. in length, soft and succulent. Some of the larger show on section a central dull red area surrounded by a zone of yellowish-gray color. The ileo-colic glands are enlarged.

The kidneys together weigh 200 gm. The capsule tears away readily and leaves a smooth pale surface thickly studded with bright red ecchymotic points. Throughout the cortex are minute hæmorrhages. Several small ecchymoses are seen below the mucosa of the bladder. The bone marrow of the femur is of deep red color. The other organs are normal.

Microscopical Examination.—The liver contains scattered foci of necrosis within which are proliferated cells with round or irregular nuclei. The sinuses of the mesenteric and retroperitoneal lymphatic glands are distended with large cells of an epithelioid type, many of which contain ingested lymphocytes. In places these cells are necrotic and their nuclei no longer stain. Sections through several Peyer's patches of the lower ileum show no hyperplasia nor is there any infiltration of the muscularis with lymphoid cells. In some sections are found collections of a few large cells of an epithelioid type. The solitary follicles of the large intestine appear to be normal.

Bacteriological Examination.—Agar-agar plate cultures were made from the heart's blood, lung, liver, gall-bladder, spleen and kidney. The bacillus coli communis was obtained from the liver and kidney. From the liver, gall-bladder and kidney was obtained a motile bacillus of similar morphology and cultural characters but with the following peculiarities:

On potato a moist glistening appearance is noticeable at the end of twenty-four hours; at the end of two days the growth is visible as a thin yellowish-white film. Control cultures of the typhoid bacillus from other sources showed a similar growth upon potato of the same stock. Milk tinted with litmus is slightly acidified and is not coagulated. In litmus whey (Petrusevsky's medium) at the end of seven days, the acid formed in 10 cc. of the medium is equivalent to 0.6 cc. of one-tenth normal sodium hydroxide solution. Grown in glucose agar-agar the organism forms no gas. Tested in fermentation tubes it formed no gas with glucose, lactose or saccharose; with glucose the reaction of the medium was acid at the end of forty-eight hours, while with lactose and saccharose an alkaline reaction was retained. Indol was

not formed in Dunham's solution at the end of a week. Tested with the blood serum of a typhoid patient giving the agglutination reaction with a typhoid bacillus from another source, a positive agglutination test was obtained; with serum diluted 1 to 200 the reaction began in 5 to 10 minutes and clumping and cessation of motility was complete in 30 to 60 minutes. The organism gave the same reaction when tested with the blood serum of a rabbit immunized to the typhoid bacillus; with serum diluted 1 to 200 clumping occurred in 15 to 30 minutes. The characteristics enumerated serve to identify the organism as the typhoid bacillus.

The case resembles those which have been reported as instances of typhoid infection without intestinal lesions. The clinical course was that of typhoid fever; during the first two weeks rose-spots were present, the spleen was enlarged and the temperature curve was that usually observed. A positive Widal reaction confirmed the diagnosis. The disease did not appear to be of a very severe type until the occurrence of repeated hæmorrhage, persistent epistaxis, purpuric ecchymoses, and hæmorrhage from the bowel, finally producing grave secondary anæmia. At autopsy the usual intestinal lesions of typhoid fever were not found; there was no ulceration of the mucosa and the Peyer's patches and solitary follicles were so slightly changed that the alterations present might readily have been overlooked had not typhoid infection been suspected. The solitary follicles of the large intestine were marked by minute points of pigmentation. The history gives evidence that the intestine was implicated early in the disease since during the first and second weeks there were diarrhœa, abdominal pain and tenderness, and some distention. The presence of blood in the stools during the last week, in association with hæmorrhage from the nose and into the subcutaneous, subserous and subcutaneous tissues, was not the result of ulceration since careful examination showed the mucosa to be everywhere intact. In part at least the changed blood in the stools may have been swallowed from the nose. Though the intestinal lesions of typhoid were almost entirely absent, the mesenteric lymphatic glands and the spleen were enlarged and the liver contained foci of necrosis. The bacteriological examination of the case is sufficiently complete to demonstrate that the child died with typhoid fever complicated by a condition resembling purpura hæmorrhagica; the case is one of hæmorrhagic typhoid fever.

The disease did not run its course without intestinal lesions. The early diarrhœa and abdominal pain, the enlargement of the mesenteric lymphatic glands, the slight swelling of the Peyer's patches and solitary follicles of the small intestine and the presence of minute points of pigmentation upon the solitary follicles of the large intestine indicate that the intestine was not wholly unaffected. These lesions were slight and at the time of death had almost completely subsided. Doubtless hyperplasia of the lymphatic apparatus of the intestinal wall was more marked during the first weeks of the disease.

The number of cases of so-called typhoid fever without intestinal lesion is not large. The earlier cases are collected by Chiari and Kraus,² who have recorded six instances of what they regard as pure typhoid septicæmia, invasion of the internal organs without demonstrable intestinal lesion. Flexner and Harris³ reviewing the literature regard as doubtful the earlier cases, those of Banti,⁴ Karlinski⁵ and Guarnieri,⁶ since the means of identifying the typhoid bacillus then available are inconclusive. Ophüls⁷ has in the last year again reviewed this literature. In some of the reported cases he believes the organism entered the body by the usual path, while in others the published reports do not exclude the possibility that lesions were present but subsequently subsided. He thinks that the necessary means now at our disposal for the differential diagnosis between the typhoid bacillus and allied forms were employed only in the case of Flexner and Harris, in the three cases of Lartigau⁸ and in the one reported by himself.

Cases reported as instances of typhoid fever without lesions of the intestine fall into several groups. (a) In many cases the typhoid bacillus has not been identified with certainty so that the nature of the disease is doubtful. (b) In some of the cases which are cited as examples of the condition slight lesions of the intestine are described. (c) Primary tuberculous ulceration of the intestine has, it appears in at least three cases, afforded a portal of entry for the typhoid bacillus, characteristic intestinal lesions of typhoid fever being absent. (d) Death may have occurred so long after the onset of the disease that opportunity has been given for the subsidence of preexisting lesions. (e) In a small number of cases death has occurred during the first four weeks of the disease and careful bacteriological examination has demonstrated the presence of the typhoid bacillus in the organs after death.

Though we cannot deny the possibility that typhoid fever may occur without lesions of the intestine, much of the evidence furnished by the published reports is inconclusive. In many reported instances the demonstration of the typhoid bacillus has been incomplete, insufficient means having been used to identify it. The cases of Banti and of Guarnieri, as stated by Flexner and Harris, belong to a period at which the difficulty of separating the typhoid bacillus from allied forms was not recognized.

Karlinski⁹ has recorded three cases of typhoid fever without intestinal lesion, certainly a rare condition, all of which were under observation within a period of two months. The

² Zeitsch. f. Heilkunde, 1897, xviii, p. 471.

³ Bulletin of the Johns Hopkins Hospital, 1897, viii, p. 259.

⁴ Riforma medica, 1887; Ref. Baumgarten's Jahresbericht, 1888, iv, p. 148.

⁵ Wiener med. Wochenschr., 1891, xli, pp. 469, 511.

⁶ Riv. gen. di clin. med.; Ref. Baumgarten's Jahresbericht, 1892, viii, p. 234.

⁷ New York Med. Jour., 1900, lxxi, p. 728.

⁸ Bulletin of the Johns Hopkins Hospital, 1899, x, p. 55, and New York Med. Jour., 1899, lxx, p. 158.

⁹ Loc. cit.

first two cases which were admitted to the same ward within a few days died on the twenty-third and twenty-second day of their disease. The third patient, who was convalescent from a minor operation upon the finger, acted as an attendant upon the first two and subsequently contracted a similar disease. The clinical course in none of these patients resembled typhoid fever, and of the second in which a rash resembling rose-spots was present upon the trunk, neck and extremities, Karlinski states that had he not found the typhoid bacillus in the organs after death he would have regarded the case as one of typhus fever. In the three cases the spleen was very greatly enlarged but, except in the third, no intestinal lesions were found. In the lower ileum of the third patient, who died on the seventeenth day of his illness, four pigmented scars were present and these Karlinski thinks were the results of typhoid fever, but since the patient died during the third week it is improbable that they represented healed ulcers occurring during the fatal attack. From the spleen of all the cases and from other organs in the second and third Karlinski cultivated an organism which he believed to be the typhoid bacillus. The same organism he states was found repeatedly during life in blood from the third patient. As a means of identifying the typhoid bacillus Karlinski depended upon the character of the growth on potato, in the light of our present knowledge a very uncertain method. It seems probable that the three cases which Karlinski regarded as typhoid septicaemia were in reality, as he himself suggests, instances of typhus fever.

Beatty¹⁰ describes the case of a man who suffered for six days with hæmaturia and jaundice. The intestine presented nothing abnormal. He mentions without details that the typhoid bacillus was found at autopsy and concludes that this case as well as a second resembling it but with no bacteriological examination, were instances of typhoid fever without intestinal lesions. In three of the six cases which Chiari and Kraus regard as instances of pure typhoid septicaemia the typhoid bacillus was not isolated from the organs, though a positive Widal reaction was obtained with the blood serum.

DuCazal¹¹ has recorded the case of a man who died with double pneumonia on the twenty-first day of his illness. The clinical course resembled that of typhoid fever; rose-spots were present and before death were extraordinarily confluent over the thorax and abdomen. The abdomen was greatly distended but there was no tenderness. At autopsy the spleen was much enlarged but there was no alteration of the intestine nor of the mesenteric lymphatic glands. From the spleen was obtained an organism having the cultural properties of the typhoid bacillus, but in the absence of the agglutination test its identity may be doubted. The patient of Pick¹² died on the twenty-fourth day of his illness; a positive agglutination reaction was obtained with the blood serum. No intestinal lesions were noted nor was the spleen enlarged, but the

author states without giving details that the bacteriological examination demonstrated a typhoid infection.

The reports of several instances of so-called typhoid fever without implication of the intestine show that slight lesions were present. To this group belongs the case of Nicholls and Keenan.¹³ The solitary follicles of the ileum were swollen, congested and of slaty color; the Peyer's patches were enlarged. The recently reported case of Ophüls¹⁴ was not entirely without lesions of the intestine. The appendix vermiformis was the seat of well marked inflammation, and microscopic examination showed hyperæmia and enlargement of the lymphatic follicles; the epithelium was absent in places. Atypical cases of typhoid fever with only a single intestinal ulcer occur. Chiari and Kraus cite such a case reported by Banti.

Of considerable interest are several cases in which the typhoid bacillus was demonstrated in the organs, and though there were no characteristic intestinal lesions of typhoid fever the intestine was the seat of tuberculous ulceration. They seem to show that the typhoid bacillus can enter the body through pre-existing lesions of the intestinal canal. Guinon and Meunier¹⁵ describe the case of a boy, eight years of age, who came under observation with symptoms of pulmonary tuberculosis. After several days rose-spots appeared, the temperature curve assumed the character present in typhoid fever and a positive Widal reaction was obtained. The autopsy disclosed generalized tuberculosis and tuberculous ulcers were found in the intestine. The typhoid bacillus was isolated from the spleen, from fluid in the pleura and from the lung. Lesions of typhoid fever were not found. Chiari and Kraus record two similar cases occurring in adults. Death occurred with chronic pulmonary tuberculosis, and tuberculous ulcers were present in the intestine but there were no lesions of typhoid fever. In the first case the typhoid bacillus was obtained from the gall-bladder and from the enlarged lymphatic glands, while in the second case the same organism was grown from the gall-bladder though cultures from the other organs remained sterile. In the latter case the blood serum during life diluted 1 to 10 agglutinated the typhoid bacillus, that from the femoral vein at autopsy diluted 1 to 20 produced the same effect. Such cases cannot be grouped with those in which the intestine appears to be healthy, since it is probable that the pre-existing intestinal lesion was the portal of entry for the organism.

In a certain proportion of the published cases the clinical history, the presence of the Widal reaction during life and the demonstration of the typhoid bacillus in the organs after death leave little doubt of the existence of typhoid infection though the intestine appeared to be normal. Doubtless many cases of typhoid fever run their course without intestinal ulceration, the primary hyperplasia of the lymphatic follicles subsiding without any loss of substance. Chiari and Kraus in

¹⁰ Dublin Jour. of Med. Science, 1897, 3rd ser. cccii., p. 97.

¹¹ Bull. et mém. de la Soc. méd. des Hop. de Paris, 1893, 3 s., x, p. 243.

¹² Wiener klin. Wochenschr., 1897, x, p. 82.

¹³ Montreal Med. Jour., 1898, xxvii, p. 9.

¹⁴ Loc. cit.

¹⁵ Le Bulletin médicale, 1897, xi, p. 313.

their article upon atypical typhoid and typhoid septicaemia record three cases in which death occurred with broncho-pneumonia during the third or fourth week; the lymphatic follicles of the intestinal wall were swollen but were not ulcerated. In several cases reported as instances of typhoid fever without lesion of the intestine death, occurring many weeks after the onset of the disease, was the result of some complication or sequela, and opportunity was given for the restitution of swollen lymphatic tissue. Since we are familiar with the persistence of the typhoid bacillus for long periods in the body, it is not surprising that the organism was demonstrated in the organs after death. To this group belongs the case of Kuhnau,¹⁶ whose patient died with suppurative nephritis and cystitis on the fifty-eighth day of her illness after having undergone an attack of facial erysipelas. In one of the cases of Chiari and Kraus death took place on the forty-third day of the disease with multiple abscesses caused by the staphylococcus pyogenes aureus; the typhoid bacillus was found only in the urinary bladder. The third case which Lartigau¹⁷ reports is that of a woman who, four months before her fatal illness, suffered with an acute febrile disease diagnosed typhoid fever. Death followed an operation for extrauterine pregnancy. The typhoid bacillus and the streptococcus pyogenes were isolated from the uterus. The case reported by Flexner and Harris¹⁸ is that of a man who died two months after the onset of his fatal illness with thrombosis of the pulmonary artery to the lower lobe of the right lung, gangrene of the lung, perforation of the pleura and pyopneumothorax. The typhoid bacillus was grown from the lung, spleen, liver and kidney.

Cases in which death occurs early in the disease can alone afford conclusive evidence that lesions of the intestine have not been present. In the case which we have described death occurred on the twenty-sixth day of the disease, yet at autopsy very little evidence of intestinal lesion was found, though there was reason to believe that the intestine had been implicated. Cheadle and Lartigau have reported cases where death occurred during the third, fourth or fifth week.

Cheadle¹⁹ reports the case of a boy three years of age. Little doubt can be entertained that he suffered with typhoid fever. A brother and a sister of the patient were coincidentally affected with the disease; rose-spots were present and the Widal reaction was obtained. There was profuse diarrhoea during the first two weeks of the illness. Death occurred on the thirty-second day. There was no ulceration of the intestine and the Peyer's patches appeared to be normal, but the mesenteric lymph glands were enlarged. Cheadle states that the typhoid bacillus was cultivated from the spleen. Lartigau has reported two very carefully studied cases in which, though death followed in three weeks the onset of symptoms, lesions of the intestine were

not found. The first case²⁰ is that of a man 36 years of age who died on the twenty-first day of his illness. There was at no time diarrhoea, abdominal pain nor tenderness. At autopsy the mesenteric lymphatic glands and the spleen were enlarged and microscopically presented the changes usually found in typhoid fever. The liver contained necrotic foci and so-called lymphoid nodules. The typhoid bacillus was carefully identified in the heart's blood, lung, liver, gall-bladder and spleen. The second case,²¹ a man 51 years of age, died during the latter part of the third week of his disease. Chronic interstitial nephritis, heart hypertrophy and broncho-pneumonia were found at autopsy. Though the intestine was free from lesion the typhoid bacillus was cultivated from the liver, gall-bladder, kidney and urine.

Few of the cases which have been cited furnish evidence that the typhoid bacillus can enter the body in the absence of intestinal lesions. In view of the cases of Cheadle and Lartigau, perhaps those of DuCazal and Pick, this possibility cannot be denied, but our case suggests that even in these, lesions may have been present at the onset of the disease. The difficulty of proving that micro-organisms enter through an exposed surface which remains healthy is obviously great, and the study of this group of cases does not conclusively prove its occurrence. On the other hand, they do not show that the organism can enter by any path other than the intestinal canal. From a histological study of the lesions of typhoid fever Mallory²² thinks it probable that the lesions of the Peyer's patches, of the mesenteric glands and of the other organs are caused by toxic products absorbed from the intestine by way of the lymphatic apparatus. Even should this explanation be accepted the group of cases which we have studied does not demonstrate beyond doubt, that these toxic products can enter without producing any lesion of the intestinal wall. They nevertheless emphasize the fact that the localization of the typhoid bacillus is not exclusively in the lymphatic apparatus of the intestine and the intestinal lesions of fatal cases may be so slight that at the time of autopsy they are no longer recognizable.

DISCUSSION.

DR. FUTCHER.—I would like to say in regard to the clinical aspect of this case that it illustrated very well the hopelessness of endeavoring to counteract the tendency to bleeding in these cases where a hæmorrhagic diathesis occurs, just as one is almost helpless in hæmophilia. We tried all the usual methods to stop the bleeding in this case; first, by attempting to increase the coagulability of the blood by calcium chloride administered internally and later by using carbonic acid gas inhalations; second, by the local treatment, such as the local application of suprarenal extract to the nostrils and the injection of a 5 per cent solution of gelatin in normal salt solution.

¹⁶ Berl. klin. Wochensh., 1896, xxxiii, p. 666.

¹⁷ New York Med. Jour., 1899, lxx, p. 158.

¹⁸ Loc. cit.

¹⁹ Lancet, 1897, ii, p. 254.

²⁰ Bulletin of the Johns Hopkins Hospital, 1899, x, p. 55.

²¹ New York Med. Jour., 1899, lxx, p. 158.

²² Journal of Experimental Medicine, 1898, Vol. iii, p. 611.

All measures failed except the packing of the nares both anteriorly and posteriorly, which was finally resorted to.

It is the second case of hæmorrhagic typhoid we have had here. When Dr. Hamburger reported the first case 685 cases of typhoid had been treated in this hospital. This case makes the second one out of a total of over 1000 cases of typhoid which have been under treatment. Its rarity is also illustrated by Ouskow's statistics which gave four deaths from hæmorrhagic diathesis in 6513 cases of typhoid fever. The hæmorrhagic diathesis may manifest itself early in the typhoid attack but more commonly it appears late in the disease. It is rather a fatal complication but some cases do recover, as did our first one.

DR. WELCH.—I think Dr. Opie's careful analysis of the reported cases covers the ground completely and brings up a number of points of interest. I was especially interested in four of the groups he specified, namely, the group in which the lesions were so slight, as in his case, that they might be readily overlooked; those in which the patient has died at a time when one might readily suppose that the intestinal lesion had healed; cases with only one or two ulcers, perhaps in an unusual situation, as in the vermiform appendix or the large

intestine; and the group in which there is a remarkable persistence of the presence of the organisms after disappearance of the intestinal lesions.

I think there is no question that cases of typhoid infection can occur without ulceration of the intestines. Clinically certain cases are so very mild that it is reasonable to think, and the idea is not a new one, that there is no actual ulceration, but merely an infiltration of the solitary follicles and Peyer's patches. Then, the persistence of the typhoid bacillus after recovery from the intestinal lesions is illustrated by a number of observations. We have had instances here of such persistence for months and indeed for years after recovery from the disease. We know now that typhoid bacilli may persist in the urine, even without any cystitis, long after the patient is apparently well, and it is certain that they may remain a long time in the gall-bladder.

In the present case a less careful pathological study would have led to its report as one entirely without intestinal lesions, and it is quite proper, I think, that Dr. Opie should express doubt, and indeed a certain degree of skepticism, whether if this very minute study had been carried out in all the cases there would not have been found in some of them some small lesion of the intestine.

FREQUENCY OF TYPHOID BACILLI IN THE BLOOD.¹

BY RUFUS I. COLE, M. D.,

Assistant Physician, The Johns Hopkins Hospital. In Charge of Bacteriology.

Following the discovery of *Bacillus typhosus* by Eberth (1) in 1880, numerous attempts were made to isolate the organism from the patient's blood. Probably the first successful attempt was that by Fränkel and Simmonds (2), who, in 1885, reported one positive result in six cases. The same year Wissokowitsch (3), by animal experimentation, showed that most bacteria, including *Bacillus typhosus*, when inoculated into the circulating blood, unless in overwhelming numbers, very quickly disappear from the blood and find lodgment, especially in the liver, spleen and bone-marrow. Following this work repeated attempts to obtain the bacilli from the blood were still made by many observers, some with long series of cases, mostly with entirely negative results. These observations in connection with the work of Wissokowitsch led to the general acceptance of the view that the typhoid bacillus entered the general circulation only very rarely and then very quickly disappeared. During the next ten years quite a number of isolated cases of typhoid septicæmia were reported in which the bacillus was isolated from the blood either during life or at autopsy.

The first series of cases in which the technique in obtaining the cultures was good, and identification of the typhoid bacil-

lus fairly certain (although agglutination was not tested), was that of Kühnau (4), who, in 1897, reported 41 cases, in 11 of which he obtained the typhoid bacillus from the blood during life. He knew of the work of Stern (5) and others on the germicidal properties of the blood, and, therefore, at once diluted the blood in 50 cc. of bouillon, and from this at once made plates, usually 20 in number. Other observers have failed to find them in so considerable a proportion of cases, so that only within the past few months, Scholz and Krause (6), in an article on the clinical value of present bacteriological methods in typhoid fever, after reviewing the work on isolation of the bacillus from the stools, urine, rose-spots, etc., state that cultures from the blood of typhoid patients are of no value for diagnosis, since only in rare cases are the bacilli found in the blood.

However, considering the wide distribution at autopsy, the frequency of the bacilli in rose-spots, as shown during the past two years by Neufeld (7), Curshmann (8) and Richardson (9) (in 32 out of 40 cases by the three observers), their frequency in the urine (in about one-fourth of the cases, as shown by Richardson (10), Gwyn (11), Horton-Smith (12) and others, my own observations being 17 times in 49 cases), and their having been found in lesions in almost every organ and bone of the body, it has seemed probable that they must

¹ Read before the Johns Hopkins Hospital Medical Society, February 4, 1901.

be present, in some stage of the disease at least, not only in the blood of the rose-spots, but in the general circulation as well.

With a knowledge of the work of the previously mentioned observers, I have, during the past few months, made a series of cultures from the circulating blood of typhoid patients. The technique briefly was as follows: The skin over the anterior surface of the arm at the bend of the elbow was carefully cleaned with green soap and water, followed by alcohol, ether, bichloride of mercury (1-1000), and a hot compress soaked in the latter solution applied for from one-half to one hour. It was found by experience that the *hot* compresses were of considerable importance in causing dilatation of the superficial veins. When ready to take cultures, the bichloride was removed by sponging with sterile water. In a few cases the skin over one of the veins was incised and vein dissected out before inserting needle. This is usually a very unnecessary procedure, giving the patient a great deal of pain and apparently increasing rather than decreasing the chances for contamination. The only case in which my cultures were contaminated was one in which this was done. By thoroughly cleaning the skin and hands of the operator and by touching the needle only with sterile forceps, never with the fingers, and by working with as little delay as possible, all danger of contamination can be avoided. Just before inserting the needle the arm is grasped tightly below the shoulder by a nurse or assistant and the needle is quickly inserted into one of the superficial veins. By using a small needle and entering the vein with one thrust there is no more pain in obtaining 8-10 cc. of blood than in the administration of a hypodermic or in the puncture of the ear. In all cases 8-10 cc. of blood were withdrawn and, after removal of the needle from the syringe, the blood was divided among a number of tubes or flasks filled with bouillon. At first tubes were used but in the last six cases, Erlenmeyer flasks, each containing 150 cc. of bouillon, were used. One to six flasks were used for each case, so that the dilution of the blood was from 1-75 to 1-150. The flasks were then shaken and placed in the incubator and after 24 hours, if cloudy, agar plates were made. Usually the organisms in the bouillon were somewhat clumped, at least sluggishly motile, and so not suitable for trying serum reaction.

The diagnosis of *Bacillus typhosus* in each case was decided by motility, staining properties, typical growth on agar, glucose agar, gelatin, litmus milk, bouillon, Dunham's peptone solution (which after one week's growth was used for indol test) and finally, agglutination by known typhoid human serum, dilution 1-50, in one hour. Frequently a fairly definite conclusion can be reached in 36 hours after obtaining the culture. If the bacilli grow out in the bouillon in 24 hours, they can be transferred at once to the various media, and from the slant agar after 6-8 hours, a suspension in bouillon can be made in which the serum reaction can be tried.

The table on opposite page gives a list of the cases from which cultures were made with the results, and also the results of urine cultures and Widal tests on the same cases.

Cultures were made from fifteen cases, in eleven of which the typhoid bacillus was cultivated. From the last seven cases in which a greater dilution of the blood was made, the bacillus was obtained every time. The cases included both those of moderate severity as well as those of great intensity. Five of the eleven cases in which the results were positive subsequently died, so that apparently cultures were taken from the more severe cases, though this was rather accidental than intentional, as they were chosen at random. Three of the cases in which the organisms were isolated had very light attacks. In one of the negative cases (VI) the cultures were contaminated with air organisms. In this case the skin was incised and vein dissected out. The child was not very ill and was removed from the hospital before a second culture could be taken. In one negative case (VII), in which cultures were taken on two occasions, the course was prolonged and of great severity. One of the other negative cases (VIII) was also one of very great severity and cultures were taken on three different occasions with a negative result each time. This patient was pregnant and aborted on the twelfth day, and the negative results are especially surprising and unfortunate since Dr. Lynch succeeded in isolating the typhoid bacillus from the blood of the fetus. This patient's urine also contained typhoid bacilli. The organisms must have been in the blood during at least a part of the time and the failure to grow is hard to understand. It may be mentioned that this was one of the earlier cases and only bouillon tubes were used in which to dilute the blood. In all of the cases, with the exception of the two last mentioned, cultures were made on but one occasion.

The positive results were obtained at various stages of the disease, most of them during the second week, the earliest on the sixth day, the latest on the twenty-seventh day, the latter being on the second day of an intercurrent relapse.

In five cases (II, IX, XII, XIII, XIV) the cultures were positive before a positive Widal test (dilution 1-50 in one hour) was obtained. In one case (XI) the record of the date of positive Widal test has been lost.

Cultures were made from the urine of twelve of the fifteen cases and the bacilli were isolated from six, two of these, however, at autopsy.

The cases were all clinically those of typhoid excepting two.

One of these (IX) was a case which developed a continuous temperature while in the hospital on the gynecological service during convalescence from an operation for pelvic inflammatory disease. The Widal reaction was positive 1-10, negative 1-50. The symptoms were those of intra-abdominal inflammation, there was a possibility of intestinal tuberculosis, and, while typhoid was suspected, the diagnosis was not at all certain. Cultures were made from the blood twenty-four hours before death and the typhoid bacillus isolated—too late however to make the diagnosis during life. The autopsy showed typical intestinal lesions of typhoid.

The other (XIV) was a very acute case which entered the hospital actively delirious, with some rigidity of the neck and other signs of meningeal involvement, and with definite signs

TABLE.

Number.	Name.	Admitted day of disease.	BLOOD CULTURES.					WIDAL TEST. ¹		URINE CULTURES.		Discharged or died.	Day of disease.	REMARKS.
			Day of disease.	No. cc. blood.	Medium.	Method.	Result.	Day of disease.	Result.	Day of disease.	Result.			
I	W.	5	24	10	6 Bouillon tubes.	Vein dissected out. Plates after 24 hrs. Quite numerous colonies on 4 plates, 2 negative.	B. typhosus.	6	Positive.	20 33	Negative. Positive.	Discharged.	81	Prolonged course. Intercurrent relapse. Relapse. Blood culture on second day of intercurrent relapse.
II	Ru.	22	27	8	6 Bouillon tubes.	Agar plates from each tube after 24 hrs. Growth of 5 colonies on one plate. Others negative.	B. typhosus.	24 28 31	Negative. Suggestive. Positive.	62	Positive.	Discharged.	78	Very prolonged course. Never extremely ill.
III	Gr.	12	14	10	6 Bouillon tubes.	After 24 hrs. all tubes cloudy. Agar plates from each tube. Colonies on all plates.	B. typhosus.	13	Positive.	26	Negative.	Discharged.	79	Rather prolonged course.
IV	Rh.	9	16	8	6 Bouillon tubes.	Tubes clear after 24 hrs. Agar plates from each tube. No growth on any plates.	No growth.	11 17	Negative. Positive.	12	Negative.	Discharged.	43	Light attack. Never very ill.
V	D.	7	10	8	5 Bouillon tubes.	After 24 hrs. 2 tubes cloudy. Agar plates from all tubes. Colonies on plates from 2 tubes.	B. typhosus.	10	Positive.	Death.	15	No complications. No autopsy.
VI	M.	10	16	10	6 Bouillon tubes.	Vein dissected out. Culture obtained with much difficulty.	Contamination.	11	Positive.	Left the hospital.	18	Patient not very ill. Left before second culture could be made.
VII	Bu.	15	19	10	6 Bouillon tubes.	Agar plates after 24 hrs.	No growth.	16	Positive.	20	Negative.	Discharged.	65	Prolonged course with relapse.
VIII	Br. O.	8	9	10	7 Bouillon tubes.	Vein dissected out.	No growth.	11	Positive.	12	B. typhosus.	Discharged.	72	Severe case. Abortion. See reference in text.
				8	7 Bouillon tubes.	Skin not incised.	" "							
				8	7 Bouillon tubes.	Skin not incised.	" "							
IX	Bo.	12	16	8	6 Erlenmeyer flasks of bouillon	After 24 hrs. all flasks cloudy. Agar plates from all flasks. Colonies on all plates.	B. typhosus.	11 14	Suggestive. "	16	Negative.	Died.	17	See reference in text.
X	McC.	9	20	2	1 Erlenmeyer flask of bouillon.	Agar plates after 24 hrs. Colonies on all plates.	B. typhosus.	9	Positive.	11	Negative.	Died.	25	Severe case. Hæmorrhage, Pleurisy, Perichondritis of thyroid cartilage.
XI	Br. M.	4	10	10	4 Erlenmeyer flasks of bouillon.	Growth in one flask. Others negative.	B. typhosus.	4	Suggestive.	Discharged.	41	Light attack.
XII	R.	5	6	2	1 Erlenmeyer flask of bouillon.	Agar plates after 48 hrs.	B. typhosus.	6 14 48	Suggestive. " Positive.	21	Negative.	Discharged.	49	Attack of moderate severity.
XIII	G.	9	14	8	4 Erlenmeyer flasks of bouillon.	After 24 hrs. all flasks cloudy. Growth from all flasks.	B. typhosus.	10 18	Suggestive. Positive.	39	B. typhosus.	Discharged.	45	Attack of moderate severity.
XIV	HL.	10	11	8	3 Erlenmeyer flasks of bouillon.	Growth in all flasks.	B. typhosus.	12	Negative.	At autopsy.	B. typhosus.	Died.	11	See reference in text.
XV	Ha.	11	12	8	2 Erlenmeyer-flasks of bouillon. 5 bouillon tubes.	Growth in all flasks and tubes.	B. typhosus.	11	Positive.	At autopsy.	B. typhosus.	Died.	15	Course rapid and severe. No complications. Patient lived but four days after entrance to hospital.

¹ By positive Widal test is meant complete agglutination in one hour with a dilution of 1-50, microscopical method.

in the chest of lobar pneumonia. The Widal test was entirely negative. The history did not suggest typhoid, and, in the presence of the lung signs, it was supposed to be only a case of lobar pneumonia with marked cerebral symptoms. The patient was admitted during the evening and on the following morning spinal puncture was performed, the fluid obtained being perfectly clear and free from organisms. At the same time cultures were made from the blood. The following morning in the cultures from the blood, instead of the pneumococcus, a motile bacillus resembling the typhoid bacillus was found, which subsequently was proven to be that organism. The patient had died during the night, so that, while the diagnosis was made by the blood culture, it had been taken too late to make the diagnosis during life. The autopsy showed, in addition to lobar pneumonia, well marked intestinal lesions of typhoid fever.

In the *Deutsche medicinische Wochenschrift*, August 9, 1900, Schottmüller, in a report of a case of fever caused by a typhoid-like organism, states that in fifty cases of typhoid fever from which he made cultures of the blood during life, he was able to isolate the typhoid bacillus forty times. He does not give the technique employed in the other cases, but states that in the case reported he used solid media, using large amounts of blood, fifteen to twenty cc. A full report is to appear later.

Auerbach and Unger in *Deutsche medicinische Wochenschrift* of December 6, 1900, also report a series of ten cases of typhoid in which cultures were made from the blood during life, the typhoid bacillus being isolated from seven of these cases. They also used fluid media and used quite small amounts of blood.

From all the results given, it is apparent that typhoid bacilli occur in the blood with much greater frequency and during a much longer time through the course of the disease than was formerly supposed. The conditions which favor their presence, why they are found at times in mild cases and are absent in more severe ones, are questions which must yet be solved. That cultures from the blood in typhoid fever have very definite clinical importance, especially where the Widal reaction is delayed, as is so often the case, is evident. From my experience, the use of considerable amounts of blood, diluting very largely in liquid media, and, on account of the

use of the latter, especial care to avoid contaminations, are the points of chief importance.

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DISCUSSION.

DR. OSLER.—One of the cases recorded illustrates, I think, that this method will prove to be of considerable value; I do not think that by any other means the diagnosis could have been made on the young colored girl admitted at the end of the first week with no rose-spots and nothing upon which to base a diagnosis of typhoid fever. The one thing evident was, that she had a violent, acute infection of some kind. The cultures made on the morning of admission would have given us the diagnosis positively within 24 hours, but unfortunately, in this case, the patient succumbed to the disease the same day. The earliest date in which bacilli were found was the 6th day of the disease. The number of bacilli, however, could not be determined.

DR. WELCH.—That is a misfortune of the method. The statement has been made that the Widal reaction is most likely to be absent when there are many bacteria in the blood. It has been contended by some that there is an antagonism between a large number of bacilli circulating in the blood and the Widal reaction.

DR. COLE.—In six of the cultures the bacilli were found in the blood before the Widal reaction was present.

A PORTABLE OPERATING OUTFIT.

By J. M. T. FINNEY, M. D.,

Associate Professor of Surgery in the Johns Hopkins Medical School,

AND

OMAR PANCOAST, M. D.

Every surgeon who has been compelled to operate often in private houses, sometimes several hundred miles from any large hospital, appreciates fully the difficulties of the problem:

how shall we manage to preserve a careful technique and approach the methods of a hospital operating room without too great expense, delay and inconvenience? In order to

remind the general practitioner of some of the chief difficulties, it may be well to mention some of the many sources of delay and vexation.



FIG. 1.

flights of stairs away; of two smaller tables placed together, frequently of uneven heights and much too broad; or of an ironing board placed insecurely on the backs of chairs or on small tables. All of these things may have to be brought from distant parts of the house and are frequently needed for other purposes, such as to hold supplies, basins, etc. Another frequent difficulty is an insufficient supply of clean basins to contain the various solutions necessary for hand disinfection, instruments, etc. It may become necessary to borrow from the neighbors and often to waste considerable time in rendering them fit for surgical use.

For a long time we have been in the habit of always taking a trunk with us to carry the necessary supplies and basins, but as the basins in regular hospital use are not generally of such sizes as to be easily and closely packed, we have often

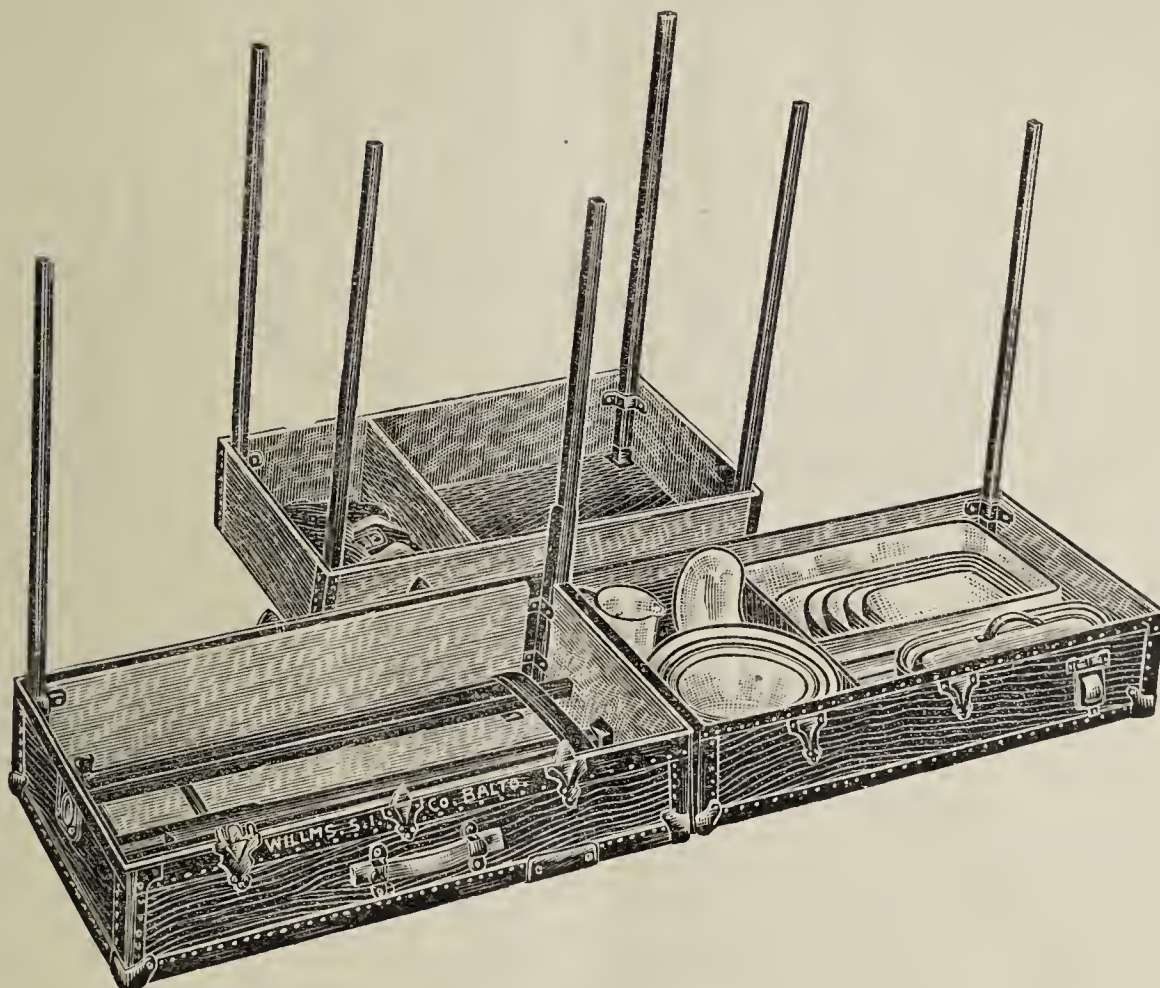


FIG. 2.

The surgeon of course carries with him a supply of instruments, dressings, materials for anesthetizing the patient and for preparing the field of operation. Sometimes these are carried in a trunk, sometimes in a hand-bag or telescope-satchel or in several such satchels.

On arriving at the house of the patient usually one first endeavors to procure something that will do service as an operating table. For any major operation the table should answer the following requirements: It should be sufficiently strong; it should be sufficiently high, so that one should not be compelled to stoop; it should be so narrow that the operator and assistant may stand on opposite sides and work in a comfortable unstrained position.

As a rule, one finds himself compelled to make use, either of the kitchen table, broad and low and perhaps several

considered the advisability of obtaining a complete set of basins for outside work and then having a trunk made to contain them, the instrument kettle and various necessary supplies, all in separate compartments to prevent shifting when the trunk is roughly handled.

In the trunk we present to-night we have accomplished these purposes and in addition have been able to add three very useful features. We have had the trunk so constructed that it can be readily converted into a very satisfactory table; we have had the tray so made that it forms a perfectly suitable table for instruments or basins; and we have also had made a skeleton Trendelenburg which when extended and covered with canvas may be placed on the trunk-table, converting it into a Trendelenburg operating table. We have accomplished these purposes by having the depth of the trunk increased

but two inches beyond that required for the ordinary supplies. The exact methods by which we obtain these results are made clear by the accompanying illustrations.

A few words perhaps are necessary to explain our method of using this outfit.

bichloride solution and the smallest of this set is sterilized by soaking in the same manner. The large basin is finally used for the operator's hand-basin of bichloride and the small one for sterile water, salt solution or sponges as the occasion requires. Two of the round basins are used for the saturated

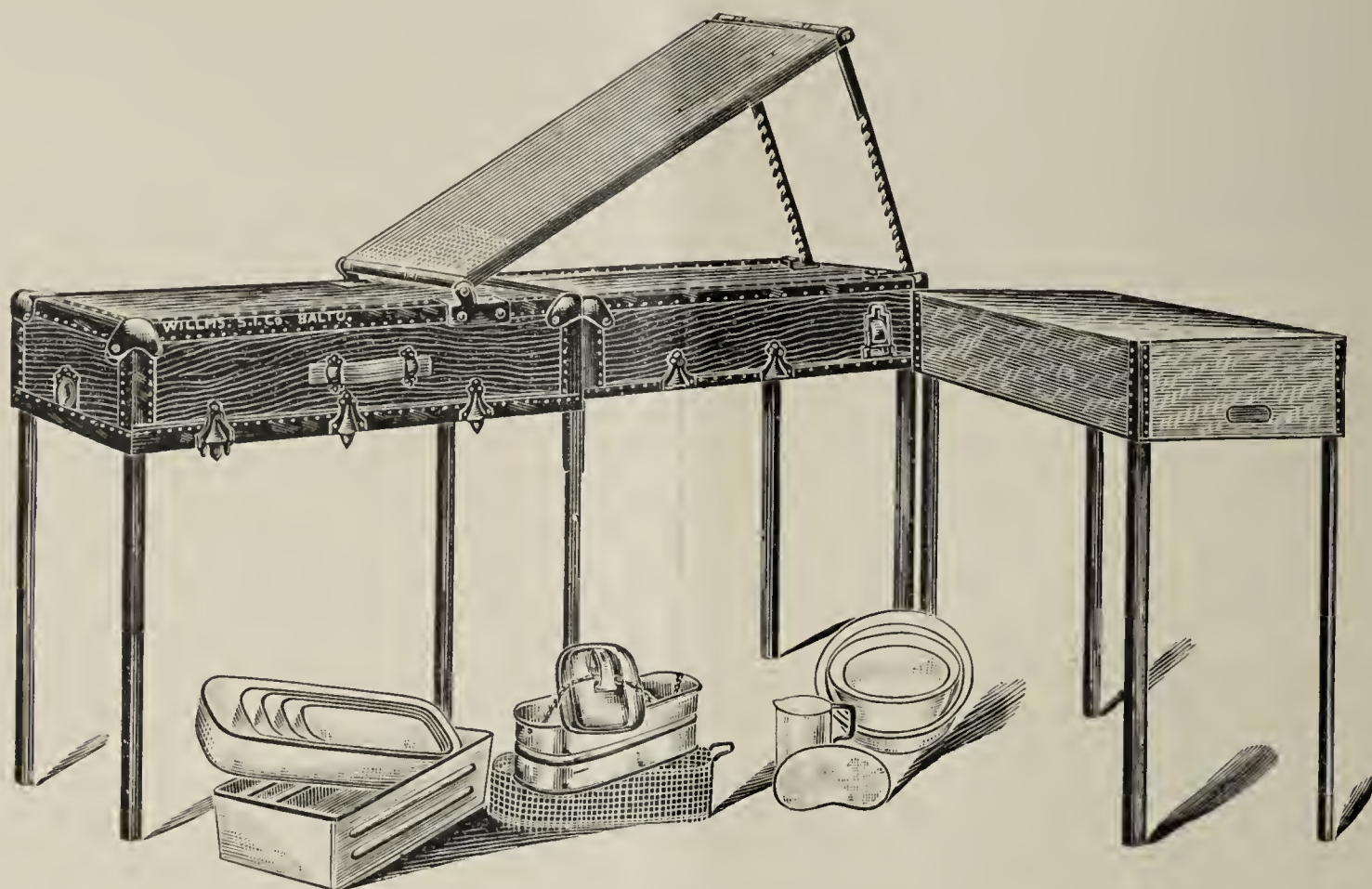


FIG. 3.

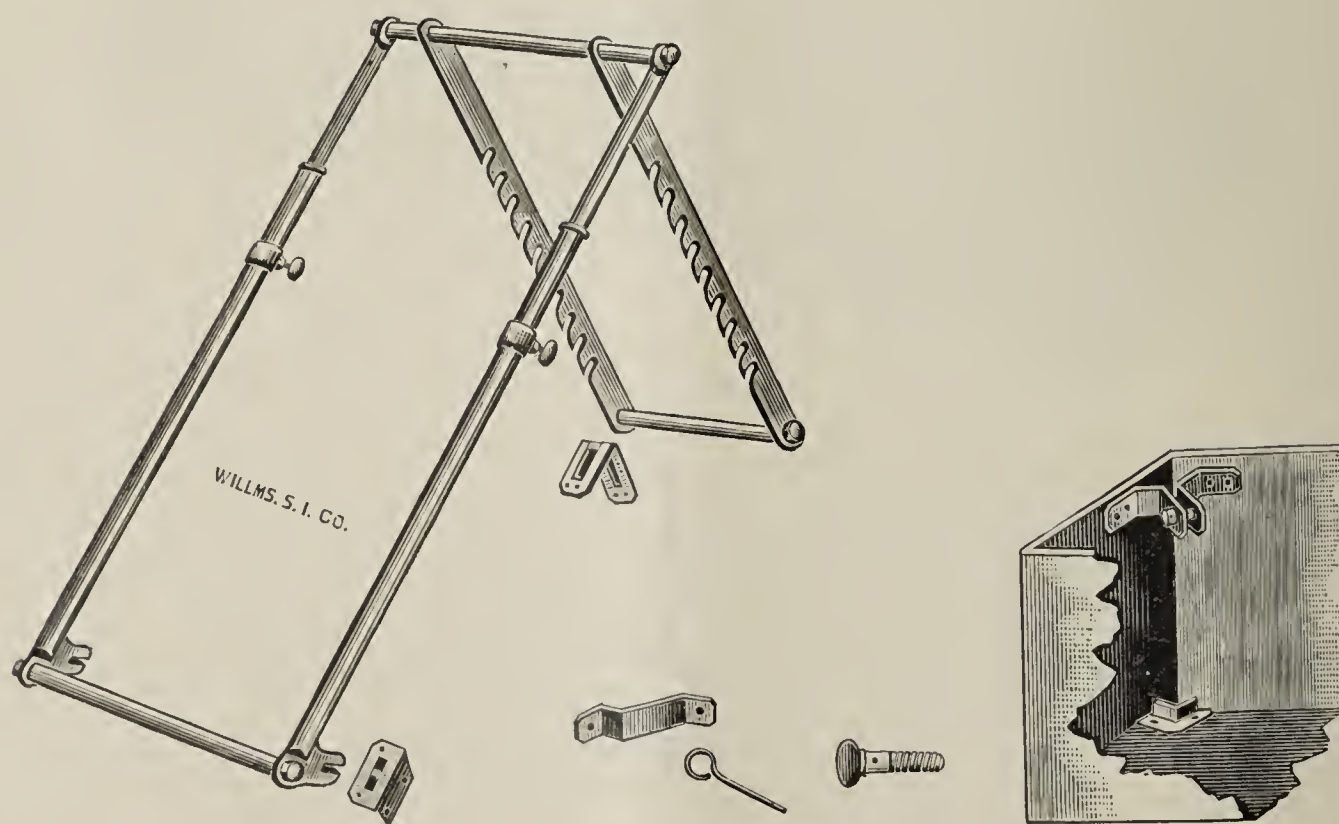


FIG. 4.

The large arm basin containing four or five instrument trays is immediately filled with a 1-1000 solution of bichloride of mercury and the trays are thus sterilized by soaking. When taken out each may be covered with a sterile towel or tray cover. The largest of the round basins is filled with

solutions of permanganate of potash and oxalic acid. The remaining one is for the soap and water used in shaving and cleaning the site of operation. The instruments are carried packed in the kettle and so may be boiled at once.

In order to form a rigid table the trunk when open is

securely fastened in this position by a thumb screw, as shown in the figure. The legs after insertion may be clasped very tightly by a few turns of the screw which regulates the size of the opening in the corner castings.

The table is usually covered with a folded blanket, mackintosh, sheet, and a Kelly or Morrison pad which drains into a bucket on the floor. When the Trendelenburg is used the trunk is protected by a mackintosh alone, while a pillow is placed over the cross rod of the Trendelenburg to protect the patient's head and shoulders.

The various chemicals necessary are carried in ordinary mailing cases so as to avoid the danger of breakage when glass bottles are carried. We use the wooden cases with screw top after carefully washing them and removing the wadding and paraffin. Sterile concentrated salt solution, cocaine, etc., are carried in bottles in mailing cases and are previously sterilized by the following process: A cork is put lightly in the bottle containing the solution and the whole top of the bottle and cork are then covered with an absorbent-cotton shield fastened around the neck of the bottle. After

sterilization the cork is pushed home through the cotton and the solution remains sterile indefinitely.

In conclusion we beg to express the hope that this trunk may be of service to other surgeons and be one means of introducing a more perfect technique in "outside" operations.

FINNEY-PANCOAST OPERATING TRUNK.

Dimensions of Trunk closed, 35" long, 18 $\frac{3}{4}$ " wide, 15 $\frac{1}{4}$ " high.

" " " as table, 70" " 18 $\frac{3}{4}$ " " 35" "

" " Tray " " 31 $\frac{1}{4}$ " " 16 $\frac{5}{8}$ " " 34" "

Trendelenburg. Length closed, 31"

" " open, 41 $\frac{1}{2}$ "

" Width, 17"

" Height of Elevation, 21"

Weight of Trunk with Tray, 60 $\frac{1}{2}$ lbs.

" " Trendelenburg with Canvas, 13 $\frac{1}{4}$ lbs.

" " Tray, 9 $\frac{1}{2}$ lbs.

" " Legs for Trunk, 8 $\frac{1}{4}$ lbs. }

" " " " Tray, 4 $\frac{1}{4}$ lbs. } 12 $\frac{1}{2}$ lbs.

" " { Full set of Basins, }

" " { Instrument Trays, } 27 lbs.

" " { Boiler, &c. }

" " Rubber Sheetting, 2 $\frac{1}{4}$ lbs.

Gross weight of Trunk and contents, 115 $\frac{1}{2}$ lbs.

ULCER OF THE STOMACH CAUSED BY THE DIPHTHERIA BACILLUS.¹

BY WILLIAM R. STOKES, M. D.

Although the diphtheria bacillus has been known as the cause of various inflammations of the respiratory tract for some little time, yet it has but recently been described in connection with such atypical conditions as diphtheritic inflammation of the conjunctiva and the external auditory meatus. Diphtheritic infection of wounds of the skin and diphtheritic vulvo-vaginitis have also been observed, but these rare infections are all completely described in "Osler's Practice of Medicine," or in Baginsky's article on Diphtheria in "Nothnagel's Specielle Pathologie and Therapie."

Schoedel (1) has recently reported a case of fibrinous inflammation of the gastric mucous membrane, due to the diphtheria bacillus, and as I have also found a gastric ulcer caused by this organism at the autopsy in a case of proven tonsillar diphtheria, I shall first refer to Schoedel's (1) article somewhat in detail.

This writer first reviews the literature, mentioning the fact that Klebs (2) and Loeffler (3) have both described cases of gastric diphtheria, in which they demonstrated their bacilli in stained sections. Wright (4) also found diphtheria bacilli in the stomach in two out of fourteen autopsies on diphtheria.

Schoedel's case was that of a child who died of faucial diphtheria without any gastric symptoms. The uvula contained a grayish membrane, but the esophagus was normal. The mucous membrane of the stomach was very red and covered here and there with a gray adherent membrane. The lymphatic structures of the intestine were swollen. A culture

from the membrane made on Loeffler's blood serum showed a large number of typical diphtheria bacilli, and these were also demonstrated in stained sections. This writer also found virulent diphtheria bacilli in the stomach of two children, dead from diphtheria, and in one of eight cases he was able to demonstrate the bacillus in cultures from the feces by means of its typical bipolar stain.

Schoedel thinks that the acid gastric juice can usually destroy a small number of diphtheria bacilli when they are swallowed, and that primary diphtheria of the stomach is thus well nigh impossible. In cases of widespread diphtheria, however, when the gastric acid is lessened in amount, large numbers of diphtheria bacilli are apt to bring about some local lesion of the mucous membrane of the stomach, when once swallowed. Although these cases are not usually detected at the bedside, their existence should not be lost sight of by the clinician.

The case which I desire to describe occurred in November, 1900, and as the young man was picked up off the streets suffering from well-marked diphtheria and housed in a vacant room in the Health Department, the clinical history is necessarily meager. All that could be obtained, however, was recorded, and I am indebted to Dr. C. Hampson Jones, Assistant Commissioner of Health, for his clinical report upon the case.

CLINICAL REPORT.

The patient was found on the streets and was referred to the Department of Health for treatment, owing to the fact that there is no infectious hospital in the city.

¹ Read before the Johns Hopkins Medical Society, January 21, 1901.

Cultures taken from the throat on two separate occasions showed the presence of diphtheria bacilli. A cot was provided for the patient in a vacant room and a nurse was placed on duty.

The fever remained high for several days, and the membrane gradually disappeared from the tonsils, as the patient received 10,000 units of antitoxin in about four days. About the sixth day of treatment, and when the membrane had almost disappeared from the throat, the temperature fell, and even became subnormal. The patient also complained of pain and hyperæsthesia in the epigastric region, and died about ten days after being admitted for treatment at the Health Department. It was impossible to find out how long the patient had suffered from diphtheria before he was seen at the Health Office.

REPORT UPON AUTOPSY.

The autopsy was performed by Prof. N. G. Keirle, Medical Examiner, who has kindly allowed me to use his notes.

Post-mortem held at the morgue on November 18, 1900. R—S—. Age twenty-three years. Ante-mortem statement. History of epilepsy. Autopsy record. Inspection. Yellow pseudo-membrane on fauces, velum and right tonsil.

Brain.—Hyperemia and edema. Pia thickened and adherent to corpus callosum, which it tears on removal.

Lungs.—Hyperemic. They ooze freely a frothy blood-stained serum. The lower lobe of the right lung is solidified. This solidification was not exactly that of lobar pneumonia, but consisted of large solidified areas, separated by a looser edematous tissue in places almost normal in appearance. The pleura was smooth.

Heart.—Normal. Hemoglobin staining of the intima of the aorta and pulmonary arteries.

Liver.—Fatty, and kidneys coarse, thick and yellow.

Cortex shows cloudy swelling.

Stomach.—This shows an ulcer two and a half cm. by one cm. near the pylorus in the most dependent portion of the greater curvature of the stomach. It is covered with a dark yellow membrane, in places almost black. The surface is necrotic beneath. The rest of the mucous membrane of the stomach was normal in appearance, and the intestines were also normal.

Cause of Death.—Septicemia of diphtheritic origin.

HISTOLOGIC DESCRIPTION.

Before describing the interesting changes which were found in the stomach, a brief report upon the changes in the various other tissues and viscera will be given.

The Right Tonsil.—The right tonsil when stained by hematoxylin and eosin shows a well-marked dilatation and congestion of the numerous blood spaces present throughout the organ. These are packed full of red blood corpuscles, and are often dilated to the size of a small vein. They are very numerous, and are usually simply surrounded by a single layer of endothelial cells. The normal stratified epithelium has disappeared over a large portion of the surface of the

tonsil, and this loss of substance ends rather abruptly at one side of the section in normal epithelium. The epithelial cells are simply replaced by a thin band of connective tissue containing many round, oval or spindle-shaped newly formed connective-tissue cells. There are few, if any, pus cells and no fibrin present, and beneath this newly formed tissue the lymphoid masses of the normal tonsil can be seen. The entire appearance is that of healing inflammation of the surface of the tonsil.

On staining the tonsil by Weigert's bacterial stain a moderate number of foci of bacteria can be demonstrated on the surface. These consist both of bacilli and cocci. These cocci probably are the staphylococcus pyogenes aureus, and they must have entered the circulation from this area, as a few colonies of a similar organism were found in the spleen and blood of the heart by cultures on blood serum. The bacilli are specimens of diphtheria bacilli, as demonstrated by cultures. Stained sections of the other tonsil showed nothing of interest.

OTHER VISCERA.

There is a well-marked, cloudy swelling of the liver present, but no other changes are noted in this organ. The kidney shows pronounced congestion of the capillaries, both between the tubules and in the glomeruli of the capillaries, and a few hyaline and granular casts are present in the tubules. The spleen shows slight congestion, and the splenic spaces are distended by proliferated endothelial cells. The heart muscle and brain show nothing unusual. No bacteria could be stained in any of these organs.

LUNGS.

Sections taken from the more solid areas mentioned in connection with the lung showed the following condition:

The small blood-vessels and veins show well-marked congestion, and the air cells are usually filled with an edematous fluid often containing many pus cells. In some areas the pus cells entirely fill up the air sacs, causing an appearance similar to that seen in the stage of gray hepatization in lobar pneumonia. The bronchi are normal, and there is no fibrin present. In specimens stained by Weigert's method a moderate number of diphtheria bacilli can be seen both in the edematous fluid, and in the more densely packed masses of pus cells. Some of these bacilli are within the protoplasm of the neutrophilic leucocytes. There are also present a large number of short chains of streptococci, which were not detected in the cultures from the lung.

ILLUSTRATION SHOWING A SECTION MADE THROUGH THE EDGE OF THE GASTRIC ULCER:

The rest of the ulcer shows about the same changes, and its surface consists entirely of necrotic tissue. This tissue contains numerous diphtheria bacilli. The ulceration has only extended as far as the muscular coat, where regeneration has already begun. The hyaline degeneration of the sub-mucous coat and the eroded blood-vessel are well shown in the illustration, which also shows the necrotic tissue, and the overhanging mucous membrane.

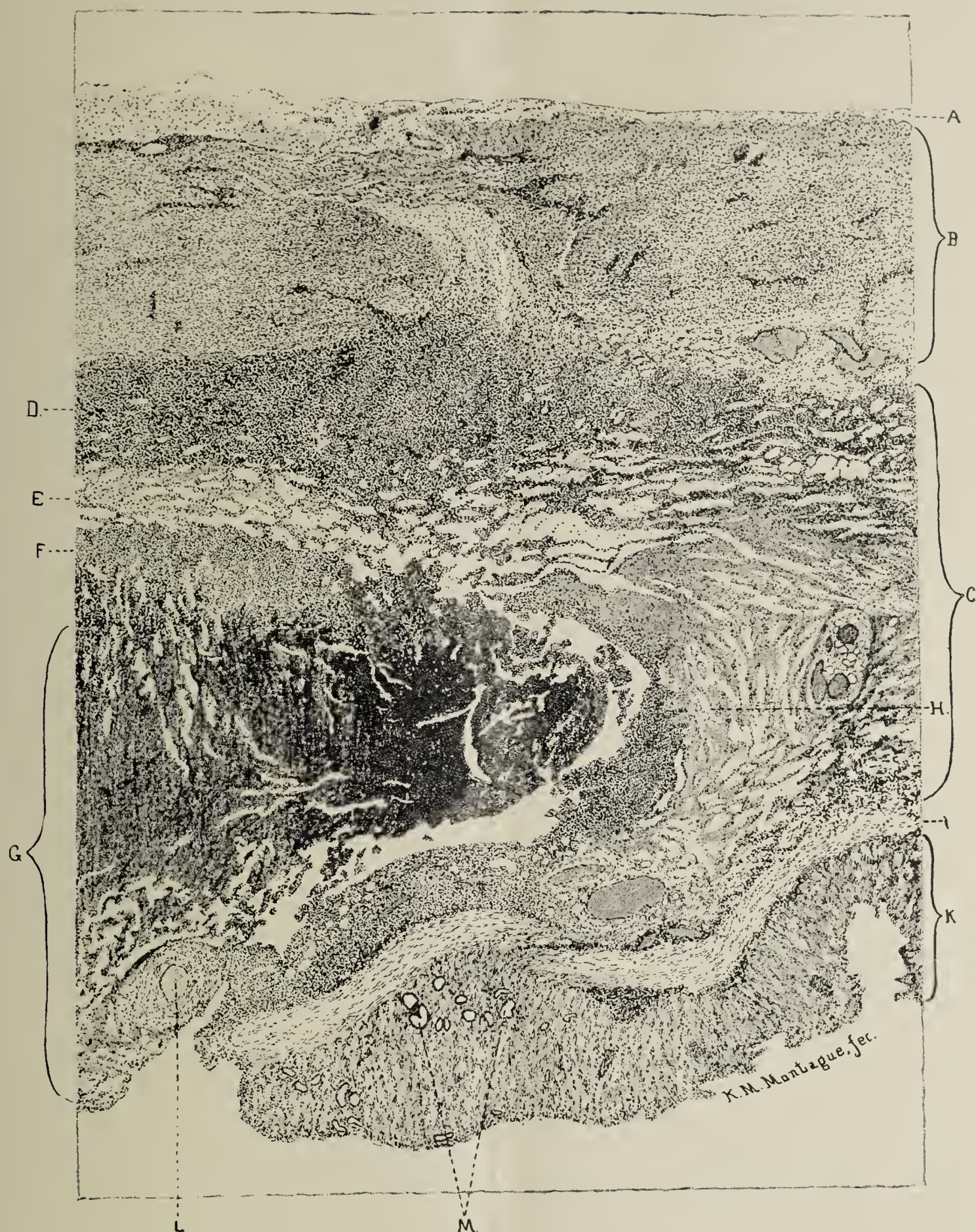


Figure No 1.

A. Peritoneal Coat.

B. Muscular Coat.

C. Submucous coat, showing superficial necrosis, hyaline degeneration, and regeneration of the base of the ulcer.

D. Layer of fibroblasts at the base of the ulcer.

E. Hyaline degeneration of the submucous coat.

F. Layer of polymorphonuclear leucocytes invading the necrotic area.

G. Superficial layer of coagulation necrosis which contains many diphtheria bacilli.

H. Hemorrhagic area in the submucous coat.

I. Muscularis mucosae ending abruptly at the margin of the ulcer.

K. Mucous coat ending abruptly at the margin of the ulcer.

L. Artery of submucous coat showing hyaline necrosis of the walls and infiltration with leucocytes.

M. Peptic glands in the mucous membrane.

STOMACH.

The ulcer of the stomach mentioned in the account of the autopsy consists of an extensive mass of coagulative necrosis, which has entirely replaced the mucous membrane. This necrotic area extends well down into the submucosa, and laterally it has undermined the mucous membrane. This overhangs the necrotic area on either side. Beyond the necrotic material, and limiting the extension of the lesion in the submucosa on either side of the ulcer, the tissue has undergone hyaline degeneration, only a few strips of connective tissue having still retained their nuclei. Portions of this hyaline tissue are dotted with small irregular hemorrhages. This thin strip of hyaline degeneration and hemorrhage extends from the sides to the bottom of the ulcer, forming its base, and separating the ulcer from the normal muscular coat beneath. That portion of the base just adjacent to the normal muscle is richly infiltrated with newly formed connective-tissue cells of various sizes and shapes, indicating the beginning of regeneration at the base of the ulcer. The base of the coagulative necrosis in the ulcer contains a moderate number of pus cells. On applying Weigert's fibrin stain no fibrin could be demonstrated in the sections.

BACTERIAL STAINS.

When the sections of the ulcer are stained for bacteria by Weigert's method, a remarkable appearance is presented. It might be remarked in passing that these sections were first stained by hematoxylin and then by eosin, according to the usual method, and after washing out the excess of eosin in water the sections are mounted on a slide and stained with gentian violet. The other well-known manipulations of Weigert's bacterial stain are then applied and the section is mounted in balsam. This triple stain differentiates all of the histological features in a satisfactory manner, while the bacteria which stain by Gram's method are clearly shown.

The diphtheria bacilli in the stained sections are limited to the necrotic material, and are more numerous on the surface of the ulcer. They are irregularly distributed throughout the entire area of necrosis, but are so densely packed together in a meshwork on the surface as to render individual inspection of bacilli impossible. Many of these organisms are very long, and some are spiral shaped. They are about the width of the diphtheria bacillus, however, and may be long forms. Most of the bacilli present the usual appearance of diphtheria bacilli in cultures, but there are some rather large square-ended organisms about the size of an anthrax bacillus, which may be unknown organisms which failed to grow in the culture from the ulcer. Even under the low power of the microscope the masses of bacilli are quite apparent on the surface, as homogeneous, or scattered blue foci. On examining the border of contact between the necrosis and the thin line of pus cells, the abrupt ending of the bacilli just at the line of contact with the neutrophilic leucocytes might well answer to the fanciful description of two armies just about to engage in a battle.

Just a few bacilli can be found on the extreme edge of the line of pus cells, and only here and there can one be found within the protoplasm of the leucocytes.

BACTERIOLOGICAL EXAMINATION.

The bacillus isolated from the right tonsil was subjected to the following tests:

A coverslip from a pure culture on blood serum was stained by Loeffler's methylene-blue, and the bipolar, or interrupted staining, was very apparent. A pure culture was obtained, and inoculated into 1 per cent lactose bouillon. This was acidulated in 24 hours. Gelatin was not liquefied, and the organism was not motile.

Cultures from the ulcer of the stomach and the lungs also contained numerous diphtheria bacilli. The liver and kidney contained many colon bacilli, and the spleen and the heart showed a few colonies of staphylococcus pyogenes aureus.

One cubic centimeter of a 24-hour bouillon culture of the bacillus isolated from the ulcer of the stomach was injected subcutaneously into the abdominal tissues of a guinea-pig. The animal died in 6 days, and the seat of inoculation showed a gray necrotic area the size of a dime. Under the microscope this area consisted of a mass of polymorphonuclear leucocytes which not only formed a thick layer on the surface of the muscle, but which have also infiltrated the abdominal muscle, forming collections of cells between the muscle bands and fibres. On staining this tissue by Weigert's method numerous diphtheria bacilli can be demonstrated. Many of these show large club-shaped ends, and in a few the bipolar stain can be seen. Cultures made on blood serum from this area gave a pure growth of the diphtheria bacillus. The lungs showed marked active congestion, but the air cells were free from any exudate. The rest of the viscera were normal.

SUMMARY.

It is a point of some interest to note that the stomach is not always able to destroy large numbers of diphtheria bacilli, especially when the powers of resistance have been lessened by an acute disease.

The ulcer which was found was certainly produced by the diphtheria bacillus, and it may appear later that these stomach lesions are not as rare as was formerly thought.

In conclusion I desire to thank Prof. N. G. Keirle for his kindness in allowing me to use his autopsy material.

LITERATURE.

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2. Verhandlung des II Congress f. inner. Med., 1883.
3. Central. f. Bak., 1887, Bd. II, No. 4.
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OVARIAN ORGANOOTHERAPY.¹

BY WILLIAM KRUSEN, M. D., Philadelphia, Pa.

The organs, tissues, and secretions of animals were extensively employed as therapeutic agents by the ancients, and constituted a prominent part of their disgusting and nauseating medicinal armamentarium. Pliny informs us that the ancient Greeks and Romans ate the testicles of the ass for the purpose of curing impotence, forestalling the later investigations of Brown-Sequard by hundreds of years. In 1852, Dr. Jackson of Philadelphia made a definite attempt to apply animal tissues to the cure of disease by administering the blood of bullocks carefully dried in vacuo, in five to ten grain doses, as a tonic. The use of glandular extracts was revived in 1889 by Brown-Sequard's advocacy of orchitic extract for impotence and certain nervous affections; and the interest was profoundly stimulated by the results which Prof. Geo. R. Murray, of the University of Durham, in 1891, obtained by the use of thyroid extract for the cure of myxedema. Since that period medical literature has been flooded with a deluge of reports of all kinds of extracts. Cerebrine, medulline, cardine, and many others too numerous to mention, have been presented to the profession, tried in the balance of practical experience and found woefully wanting. One would not be surprised to find some enterprising and energetic drug firm vaunting the merits of muscine for pugilists and athletes, or advising political spellbinders to imbibe eloquence and glosio-labial extracts at the same draught.

The popularity of this line of medication depends upon the theory of Brown-Sequard, that all glands, whether provided or not with excretory ducts, have the power to elaborate, in addition to their ordinary secretions, certain materials of unknown chemical composition, which pass into the blood and perform therein definite functions of some kind. The efficiency of thyroid extract in the treatment of myxedema and cretinism has substantiated the theory to a certain extent, but the limitations of its application remain to be determined. The animal extracts which have a particular interest for gynecologists are the uterine, mammary, parotid, thyroid, and ovarian; and of the last of these and its value it is my purpose to speak, hoping to elicit a discussion which may prove valuable to profession and patient.

In studying the action and uses of ovarian extract it is interesting to review the conclusions of Curatulo in regard to the internal secretion of the ovary. 1. The ablation of the ovaries exercises a considerable influence on metabolism. 2. The quantity of phosphates eliminated by the urine is notably diminished after the removal of the ovaries. In reality, this diminution is not due to elimination, which is the same before and after the operation, or to the diminution of the absorbent power of the intestine; for the condition in which the gastro-intestinal tract is found is the same before

as after the operation. 3. The curve of nitrogen, after ovariectomy, ascertained either by Kjeldahl's method or by Yvon's, presents a slight oscillation, without a very distinct tendency to elevation or lowering. 4. After oophorectomy the quantity of carbonic acid eliminated by the respiration, and that of the oxygen absorbed, diminish considerably up to a certain limit, from which time it remains stationary. 5. In animals from which the ovaries have been removed, the curve of the weight is progressively elevated until it attains considerable proportions from 5 to 6 months after the operation. 6. When a certain amount of ovarian juice is injected subcutaneously into sluts deprived of the ovaries, the quantity of phosphates eliminated by the urine, which diminished considerably soon after the operation, tends to increase and even to become superior to that which was ascertained before the operation; when still larger amounts are injected the quantity of phosphates increases in a very marked degree.

Hysterectomy performed in conjunction with oophorectomy does not seem to cause modifications other than those ascertained after simple removal of the ovaries. The author closes his essay with the following theory: The ovaries, like other glands of the animal economy, have, according to Brown-Sequard's general doctrine, a special internal secretion. These glands continually throw into the blood a peculiar product, the chemical composition of which is completely unknown, and the essential properties of which tend to favor the oxidation of phosphorized organic substances, of carbohydrates, and of fatty substances.

It results therefrom that, when the function of the ovaries is suppressed, whether because oophorectomy has been practiced or because the organs do not act, as is the case before puberty and after the menopause, there should be produced, on the one hand, a more considerable retention of organic phosphorus, whence there is a greater accumulation of calcareous salts in the bones; and, on the other hand, the very manifest corpulency which is ordinarily seen after oophorectomy or after the menopause.

This probably suggested the value of substitution therapy, the restoration to the diseased body of chemical substances the removal of which from the normal body gives rise to symptoms of disease. It is not necessary to review the various psychic or vasomotor disturbances which are associated with the natural and the premature menopause; they are too well known to need further comment.

Werth of Kiel was the first who made use of the ovarian treatment in troubles which accompanied the disappearance of the secretion of the ovary following either the menopause or surgical intervention. Out of ten cases, in two only did the treatment fail to bring about any result; in the other eight there was a diminution of general pains, of the headache, of the loss of appetite and sleep, of the palpitation and

¹ Read before the Johns Hopkins Medical Society, February 4, 1901.

of the feeling of anguish. Mainzer of Berlin obtained a considerable amelioration of the symptoms following double ovariectomy by administering to his patients the raw ovarian substance of the cow or the calf, in daily amounts of from 75 to 150 grains. It has been demonstrated that such large doses are not necessary. Mond has used it successfully in disorders of the natural menopause and in amenorrhea due to atrophy of the genital organs, or to neurasthenia. Spillman and Etienne also obtained good results in *chlorosis* from the administration of the fresh ovaries of sheep, of the dried ovarian substance, and of the ovarian juice. According to these authors, this treatment acted by facilitating the elimination of the toxins, increasing the red globules and causing the reappearance of menstruation. Mairat, Jayle, Touvenaint and Jouin have published observations in which this medication has led to favorable results in the treatment of amenorrhea and chloroanemia. Guerder and Vigier have found the symptoms of the natural menopause were relieved. The latter, after freeing the ovarian substance from foreign matter as fat, fibres, etc., mixed it with bicarbonate and charcoal, which preserves it indefinitely without interfering with its therapeutic effects.

Bodon (Centralblatt für Gynakologie, August, 1897) reports three cases in which he employed ovarian tablets with good effect. The third was that of a virgin, 18 years old, who had suffered with epilepsy since her first menstruation and had been under treatment for years. Bromides and other drugs had proved utterly futile. She began with one tablet daily and increased the number to ten. In the course of several months the epileptic attacks ceased; but discontinuance of the drug was followed by fresh seizures and its resumption again caused their subsidence.

Jacobs (Semaine Gynecologique, June 22, 1897), although skeptical at the beginning of his observations, had confidence in the remedy to continue its use. The extract of the ovaries of recently killed animals was used and he has tabulated 81 cases, of which only 5 are classed as failures. In one case of obesity with amenorrhea of 19 years standing, the obesity diminished and menstruation became regular. Another patient, 21 years of age, with undeveloped genitals, had never menstruated; but after taking ovarian extract for a month, menstruation appeared and has continued regularly ever since. Jacobs believes that suggestion plays a prominent part in some of these cases, though not in all. Landau (Berlin. klin. Woch., No. 25, 1896) believes that this remedy does possess the power of modifying the unpleasant phenomena of the climacteric whether physiologic or anticipated, without producing any evil effects, and that it deserves careful consideration.

Chrobak (Cent. für Gynak., No. 20, 1896) administered ovarian extract made from the fresh ovaries of cows, to a number of castrated women and had good results in two cases reported. Fosburg (British Med. Jour., April 24, 1897) gives the history of a patient who at the climacteric was much troubled with frequent and violent flushing, the face often being in a burning heat while the hands and body were icy

cold. Five grain platinoids of ovarian gland, administered 3 times daily, gave complete relief before 3 dozen were taken; and one platinoid given occasionally prevented recurrence.

Seeligman (Allg. Med. Centralzeitung, No. 3, 1898) reports 15 cases treated with extract of the ovaries of sheep and pigs, and concludes that the remedy has a decidedly beneficial effect, not only upon typical climacteric phenomena, but also upon the psychic condition and upon constitutional diseases such as gout, psoriasis, etc., which after long remaining latent develop at the menopause. Bate (Louisville Journal of Surgery, vol. v, 1898-99, p. 11) states that "physiologic action of ovarian extract as now observed is vaso-constrictor, nerve sedative, emmenagogue, and anti-anemie"; a combination of qualities which, if it truly possessed them, would make it a most valuable acquisition to our pharmacopeia.

Stimulated by such enthusiastic and gratifying clinical reports I began the use of ovarian extract, employing capsules prepared by a reliable firm, since the ingestion of raw ovaries or nauseous doses is not usually appreciated by the average American woman. For the past three years, in selected cases, in dispensary and private practice, the effort has been made to obtain some definite result from the use of this carefully prepared ovarian extract, in 3 classes of cases: (1) Those suffering from amenorrhea, dysmenorrhea and other forms of pelvic disease; (2) those suffering from symptoms following the removal of the uterine appendages, for the relief of the vasomotor changes, the flushes and cardiac neuroses which, with indescribable depression, are so often produced by the premature menopause; (3) the disturbances associated with the natural menopause. My first case was that of an intensely neurotic patient suffering from artificial menopause. Marked relief was noted for a brief period; then there was a recurrence of the symptoms. Later the patient became an adherent of Christian Science and has obtained more relief from auto-suggestion than from inspissated ovaries. Many other disappointing instances were met with. Patient after patient would faithfully take the extract to the exclusion of other remedies without any perceptible result, although occasionally the effect would be apparently so marked and the results so satisfactory as to encourage its further use. For instance, such a history as the following, taken from the case-book at St. Joseph's Hospital, would incite to renewed confidence in the efficacy of the preparation. Jan. 9, 1901, Mrs. A. C., aged 26 years, had had double ovariectomy performed by Dr. Joseph Price; general condition good, pelvic examination negative, but complained of hot flushes every few minutes and extreme nervousness. Five grain capsules of ovarian extract, 4 times daily, were ordered. The patient returned in 3 days stating that the nervousness was better and the hot flushes decreasing in frequency. In one week the nervousness had disappeared and hot flushes occurred only on exertion, two or three times daily. Another case in point was that of Mrs. J. W., patient of Dr. Chas. B. Smith of Newtown, Pa., who was operated upon for double pyosalpinx. Within 2 months after leaving the hospital she began with the usual vasomotor phenomena and relief was secured by the administration of 5-grain doses

of ovarian extract 3 times daily. Time and a regard for your patience prevent my giving a detailed history of more cases; besides the recital of our failures is never pleasant; yet it seems unfortunate that more of those who have been disappointed in their use of this product have not given their experience; only a few seem to have done so. Montgomery (*International Med. Mag.*, Nov., 1900) states that he has never seen the slightest influence from the use of ovarian extract although he has found the thyroid especially valuable in the treatment of cases of myxedema, obesity, and in some forms of sterility; and Baldy says that "a careful consideration of this subject forces one to the conclusion that it is destined quickly to follow in the steps of the testicular injections urged several years ago with the object of renewing youth." Johnstone of Cincinnati may give the correct explanation of the failure to secure more definite and satisfactory results from the use of ovarine. He says: "There is not an iota of proof that the ovary has any other function than the manufacture of eggs. The ovary is in no sense a gland. Its epithelium is arranged for the purpose of being cast out and lost, and is not placed so that its secretions, if it has any, could be absorbed either by ducts or blood-vessels. Anatomically, the ovary does not resemble the suprarenal, the thymus, or the thyroid gland. The thymus is a lymphatic gland, the thyroid and the suprarenal have a rich supply of blood-vessels so arranged that each epithelial cell is closely approximated to a venous radicle, thus providing for a rapid absorption of whatever secretion its cells may make. The ovary has a true duct, through which its epithelium, when cast out, passes off en masse to the outer world."

Probably Jacobs struck the keynote when he said that "suggestion plays a prominent part in some of these cases"; for this might explain why we have successes and failures under the same conditions without apparent cause. Not-

withstanding the many brilliant results referred to in this paper, experience leads me to the following conclusions based upon the use of the American product upon American women: (1) The employment of ovarian extract is practically harmless, as no untoward effects beyond slight nausea have been noted even when full doses have been administered. (2) In the treatment of amenorrhea and dysmenorrhea no good results were secured. (Although in some cases of amenorrhea of obesity, remarkable results have been obtained by the use of the thyroid extract.) (3) The best results were seen in the second class of cases, for the relief of symptoms of artificial menopause, when in a few instances the congestive and nervous symptoms were apparently ameliorated. (4) No appreciable result was noticed in the use of ovarine in the natural menopause. (5) No definite or exact reliance can be placed upon the drug, as it often proves absolutely valueless where most positively indicated. (6) It is extremely problematic whether, in those cases in which relief was noted, the effect was not due to mental suggestion rather than to any physiologic action of the drug. The neurotic type of individual demanding this treatment will often be relieved by any simple remedy. (7) In those instances in which effects were noted increase in dosage seemed to have little influence in maintaining the effect or preventing the patient from becoming accustomed to its use. (8) In conclusion, the theory which suggests the use of this extract seems to be at fault, and the administration of ovarine or ovarian extract is based upon a wrong assumption as to the function of the ovary. In organotherapy, the best results have been obtained from the use of the thyroid and adrenal glands, and the ovary in function is in no sense analogous to these organs. Its principal function is ovulation, and if any peculiar product is coincidentally manufactured, the isolation of this product has not yet been accomplished.

JESSE WILLIAM LAZEAR MEMORIAL.

On the 25th of September, 1900, Jesse William Lazear, at that time Acting-Assistant Surgeon in the United States Army and a member of the Government Commission for the investigation of yellow fever, lost his life from that disease at Quemados, Cuba.

Doctor Lazear was born in Baltimore County, Maryland, in 1866, and graduated from the academic department of the Johns Hopkins University in 1889. In 1892 he received the degree of M. D. from Columbia University. From 1892-95 he spent his time in study and investigation in Europe and as an interne at the Johns Hopkins Hospital in Baltimore. During the following three years and a half, while a member of the staff of the Out-Patient Department of the Johns Hopkins Hospital, he did much valuable work as a teacher and investigator in the laboratory of clinical pathology. In February, 1900, induced by the opportunity for research concerning malarial and yellow fevers, Lazear became an acting

assistant surgeon in the United States Army and was assigned special laboratory duties at Columbia Barracks, near Havana. Later, he was appointed member of a special government commission for the investigation of yellow fever. The brilliant discoveries of this commission concerning the ætiology and manner of infection of yellow fever have recently been referred to in public by a distinguished pathologist as the most important piece of work by American students since the discovery of anæsthesia. To these results Lazear, as a member of the commission, contributed largely. The final proof of their discovery that the disease is transferred by the bite of a certain mosquito, could only be obtained by direct experiment upon a human being. To this experiment Lazear, with another of the committee, courageously and heroically subjected himself, and in the performance of this noble duty he lost his life.

The many friends and admirers of the talented and accom-

plished student, of the brave, true, self-sacrificing man, desire to establish a lasting memorial to him and to his work. To this end a meeting was held on the evening of Wednesday, May 22d, which was presided over by Professor William Osler. At this meeting it was concluded that the nature of the memorial could better be decided upon when some idea could be obtained as to the amount of money available. It was, therefore, decided that a committee consisting of Dr. Stewart Paton and Dr. William S. Thayer be appointed to arrange for the distribution of a circular among the friends and admirers of Lazear, setting forth the object of the meeting. It is earnestly hoped that not only those who have

known and admired Lazear and his work, but also others, who appreciate courage and manliness and self-sacrifice, may contribute to the fund for the Jesse William Lazear Memorial.

Subscriptions may be sent to Dr. Stewart Paton, Treasurer, 213 West Monument Street, Baltimore, Md. It is to be hoped that the response to this circular may be made early, as it is hoped to be able to decide upon the nature of the memorial by the middle of June.

WILLIAM OSLER, *Chairman.*

STEWART PATON, }
WILLIAM S. THAYER, } *Committee.*

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

December 17, 1900.

The meeting was called to order by the president, Dr. W. H. Welch.

Dr. Fletcher exhibited a case of Rheumatism with Fibroid Nodules.

DISCUSSION.

DR. WELCH.—So far as I am aware, the pathology of these subcutaneous nodules in rheumatism is obscure. Some are so transitory in nature that they are probably attributable to a circumscribed inflammatory œdema; others may persist for weeks and months and are characterized by new formation of connective tissue. It has been suggested that they may be tropho-neuroses. Dr. Cheadle has called attention to the analogies between these nodules and certain fibroid nodules and thickenings of the endocardium in rheumatism. In the only specimen which I have examined the nodule contained dense, fibroid tissue, partly hyaline in character.

The Intrinsic Blood-Vessels of the Kidney and their Significance in Nephrotomy. MR. BRÖDEL.

(See page 10, BULLETIN for January, 1901.)

DISCUSSION.

DR. HUNNER.—Dr. Kelly not being present I take the liberty of reporting improved results in his operations for stone since following a definite plan for opening the kidney as outlined by Mr. Brödel.

Formerly he split the kidney, as I suppose most surgeons do to-day, along the line of greatest convexity, thus carrying the incision through the main column of cortical substance, or just that portion as shown by Mr. Brödel's drawings, which should be avoided.

I have begun experimental work upon dog's kidneys to determine the ultimate effect upon the kidney substance of different incisions and different suture materials. In the few operations I have already performed I have been able to demonstrate the value of Mr. Brödel's work as regards hæmorrhage. Cutting through the bases of the pyramids, as deter-

mined by the arrangement of the stellate veins of the surface, or in the periphery, by the lobulations, results in decidedly less hæmorrhage than follows splitting the kidney without considering these anatomical points.

DR. WELCH.—Did your investigations extend to the question of anastomosis between the renal vessels and the lumbar and ureteral vessels? It is well known that if one of the branches of the renal arteries be occluded, the area supplied by it dies, with the exception of a small zone of tissue at the base of the infarct just beneath the capsule. This is due to anastomosis with branches from the lumbar arteries.

MR. BRÖDEL.—I found these vessels very frequently but noted nothing different concerning them from what is usually stated in the books.

DR. WELCH.—Did you take up at all the question of origin of the vasa recta?

MR. BRÖDEL.—I found that these come from the vessels at the base of the pyramids and not from the glomeruli.

DR. WELCH.—I am sure that from many points of view, Mr. Brödel's communication is an important one. I am especially impressed by the number of new gross anatomical points brought out. It shows that gross human anatomy is not thoroughly worked out even yet.

A Case of Arterial Disease, possibly Periarteritis Nodosa. DR. SABIN.

(See page 195.)

January 7, 1901.

The meeting was called to order by the president, Dr. W. H. Welch.

Typhoid Infection without Lesion of the Intestine. A case of Hæmorrhagic Typhoid Fever with Atypical Intestinal Lesions. DR. OPIE and MR. BASSETT.

(See page 198.)

Report upon *B. mortiferus*. DR. HARRIS.

The history of the case from which this organism was obtained is briefly, as follows: The patient, a white man aged

44, was admitted on the 6th of October to Dr. Halsted's service. His history, both family and personal, was particularly good. Four days previous to his admission he had complained of severe headache which was followed by nausea and vomiting, the latter continuing until his entrance to the hospital. The patient fancied that the vomited material had a fecal odor, and after such spells of nausea he was unable to eat for nearly 24 hours. Two days before coming in, abdominal pain began and remained constant over the whole right side. On being asked to put his hand to the spot of greatest tenderness, he placed it to the right of the umbilicus and in the upper right quadrant of the abdomen. On the day of entry he was seized with a chill and this was followed by profuse sweating. His temperature on admission was 103° with a leucocytosis of 36,000.

On physical examination, liver dullness extended from the 6th rib 8 cm. downwards towards the central line of the abdomen. Upon palpation, the left side of the abdomen was soft and not tender or rigid. There was slight tenderness in the lower right quadrant, but no definite mass could be felt beneath the area of muscle spasm.

His condition became gradually worse, his leucocytosis varying between 7000 and 20,000, and his temperature ranging as high as 105° . On the 9th, Dr. Halsted saw the patient and advised an exploratory operation under cocaine. The condition found was this: the mass below the costal margin was the liver and upon its surface were numerous abscesses with thin walls. During the manipulation of the liver, one of these abscesses ruptured and discharged its contents into the peritoneal cavity. The abdomen was cleaned and the liver packed around with gauze to prevent any further pollution. The patient did not seem to do well, however, after the operation and the symptoms were scarcely improved in any way, though the patient stated that he felt much more comfortable. The dressings were soaked with a discharge of foul odor, the leucocytes continued to rise and later in the evening he had a chill followed by a temperature of 105° . He died on the 13th.

Coverslips made at the time of operation showed many cocci and a few bacilli with pus cells and much debris. The autopsy was performed 5 hours after death by Dr. Opie.

Cultures were made at the autopsy in the ordinary manner on plain agar and left for 48 hours before being examined. At the end of that time it was found that they had become contaminated. I then endeavored to make cultures from the abscesses in the liver. On microscopic examination of coverslips prepared from this pus I was led to believe that I had to deal with an organism that would be rather difficult to cultivate by ordinary means, so cultures were made on hydrocele fluid agar as well as on plain agar, and these were both grown aerobically and anaerobically. Both sets of the aerobic plates were entirely sterile at the end of 48 hours. On the hydrocele plates grown in hydrogen, only one showed growth, and that was the first plate made undiluted from the abscess. The plain agar plate similarly grown was sterile, although the plate showed a great deal of debris from the abscess. The

appearance of the successful plate was peculiar; surrounding three minute pieces of necrotic material were zones of very fine colony formation about 8 mm. in diameter. When viewed under the single lens these were shown to be made up of very minute colonies which were transparent and of a slightly yellowish color. Some were irregular, some oval and some round. Coverslips from these showed an organism that corresponded almost exactly with that obtained from the liver abscess material. Upon the whole, it was a very minute bacillary form occurring singly or in pairs; at times the pairs were so small that one could not positively say they were not diplococci; again were seen forms growing in chains resembling streptococci or streptobacilli. Perhaps the morphology of the bacilli from the cultures on the hydrocele fluid agar were slightly larger than those obtained directly. This was not constant, however, for cultures made later showed that the organism could grow quite as small as those found in the abscess. To make sure that I was not dealing with a contamination, cultures were made from individual colonies and it was found that no growth occurred on any media grown aerobically or anaerobically and occurred on the hydrocele agar, only, in the presence of hydrogen. From these latter, plates were again grown to rule out any chance of contamination. It was soon found that the organism would not grow upon any medium that did not contain as a basis, blood, blood-serum, or hydrocele fluid. I was unable to obtain any ascitic fluid with which to work, but it is likely that it would have grown upon that also.

The organism grown in hydrocele fluid agar was able to form gas, but that undoubtedly arose from its action upon muscle sugar. Even when dextrose-free medium was used, there was still some gas-formation. A shake culture in hydrocele-fluid-glucose-agar gave an abundant amount of gas of bad odor, almost fecal. In hydrocele fluid milk there was a slight acidification with doubtful coagulation on the fourth day and a clearing up ("peptonization") on the 6th day, until the tube became semi-transparent with a thick sediment at the bottom, made up largely of a growth of the organism. On examining very closely a hydrocele fluid bouillon culture, small bubbles of gas were noticed rising to the surface during the first 48 hours. In Dunham's medium, to which hydrocele fluid had been added, the same phenomenon was observed. The organism would not grow on Löffler's ox-blood serum.

Whilst engaged in this cultural work, experimental work was not neglected. A rabbit was inoculated with pus from the same abscess from which I obtained the organism. The animal received .3 cc. intravenously in the afternoon, and was found dead the next morning at 8 a. m. The autopsy showed nothing and cultures were negative. Sections of the tissue examined later, however, showed lesions. Another rabbit was inoculated with .4 cc. of bouillon culture, remained well for two and one-half days and then gradually weakened, became thin, and died on the 6th day. All of the animals inoculated afterwards went through the same course of gradual weakening and emaciation, but ate very well up to the

day of death, which on the average was the 6th day after inoculation. Post-mortem, the lesions of these animals were, generally speaking, emaciation, loss of subcutaneous fat and a tremendous degree of peritonitis; most of them showed a great exudation into the abdominal cavity of bloody fluid, containing much coagulated lymph. The surfaces of the intestines and abdominal organs were coated with a fibrino-purulent material. The spleen, as a rule, was usually more or less completely encased in such a sheath, and in one instance it was found with difficulty. The livers were larger than normal and were found to be studded with yellowish-white round nodules. I was not able to find the fluid contents in these experimental abscesses, as was seen in the liver of the human subject. The consistency of the material in these abscesses was putty-like. In some of the rabbits, abscesses were found in the heart's muscle and in the cerebral hemispheres. In one guinea-pig were found lesions in the lungs quite comparable to those in the human subject, and in one of the rabbits there was a complete infarction of the spleen, due to plugging of the splenic vein.

On looking over the literature one is impressed by the lack of systematic anaërobic investigation, and, with few exceptions, what has been done is without much value. The best of the kind is that carried out by two investigators in Paris, Veillot and Zuber, which will be found, published in 1898, in the *Archiv de Médecine Expérimentales*. They isolated from a case of gangrene two very small organisms but quite unlike the one I have described. In addition, from 22 cases of appendicitis, they found anaërobic bacilli associated with bacillus coli and streptococcus; in all, I think, they isolated some 7 varieties, and in 2 cases found anaërobics in pure cultures. Likewise, a pupil of theirs, Guillemot, has since written, for his thesis, a paper, which confirms their work on these organisms, and, in addition, he describes three or four more varieties. These in no wise bear any relation to the one described this evening, for they were cultivated upon a medium we all use regularly in our laboratories, glucose-agar, and they grew on all other media, if given anaërobic surroundings; whereas the organism presented to you this evening will not grow so, but requires some such medium as hydrocele fluid, blood or blood-serum, to be added to the ordinary media before growth occurs.

The name proposed for this organism, *bacillus mortiferus*, is chosen in accordance with the ordinary classification, but, if that of Migula is used, then *bacterium mortifer* would be more proper.

DISCUSSION.

DR. WELCH.—It is certainly most fortunate that Dr. Harris had from the examination of cover-slips smeared with the fresh material an instinctive feeling, such as will be understood by experienced bacteriologists, that the delicate, unusual bacillus would be difficult to cultivate, and that it occurred to him to inoculate, among other media, tubes containing hydrocele fluid. Dr. Harris has brought conclusive evidence that the organism cultivated is identical with the

one found microscopically in the original liver, and that it is responsible for the remarkable lesions of this organ. No especial emphasis need be laid upon the consistence of the pus in the experimental abscesses produced by this bacillus in rabbits, as it is well known that the pus of rabbits usually has a putty-like or cheesy consistence.

Two Cases of Amoebic Dysentery in Children. DR. AMBERG.

(To appear later.)

January 21, 1901.

In the absence of the president, the meeting was called to order by Dr. Kelly.

Exhibition of Surgical Cases. DR. MITCHELL.

Dr. Mitchell exhibited a case where the gasserian ganglion had been excised after the method of Dr. Cushing for a patient who had suffered from facial neuralgia for thirteen years, with the effect to produce complete relief from pain.

The second case was one of operation for typhoid perforation of the intestine, with recovery.

DISCUSSION.

DR. FUTCHER.—This case interested us very much clinically, and three or four points in connection with it were of special interest in arriving at the diagnosis of perforation. The child had had a tub at 6 P. M. and had been placed back in bed. At 7.15 she suddenly cried out with intense abdominal pain. A count of the leucocytes was made about this time, on the possibility of some acute complication having taken place, and they were found to be 11,500. The child complained slightly of the pain during the evening but about 11 o'clock when Dr. McCrae was making the late visit in the wards, the patient again cried out with intense pain. He called me and we went over the case together. At that time the abdomen was moderately distended, there was distinct rigidity of the muscles and slight muscle spasm. The liver dullness extended only to a point 3 cm. above the costal margin; before this it had extended quite to the margin of the ribs. The child had a peculiar facial expression, the mouth was rather puckered up and while examining her she suffered spasms of severe abdominal pain which made her cry out. A count of the leucocytes at that time showed that they had fallen to 7000. By 12 o'clock her condition had changed materially. The pulse was weaker, more rapid and of a running character; the abdominal distention was more marked; there was then definite muscle spasm and tenderness in the right iliac fossa on the slightest palpation. There was also appreciable movable dullness in the flanks. There had been practically no change in the temperature. The sudden onset of the pain and its paroxysmal character, the increased frequency in the pulse, the abdominal distention, muscle rigidity and spasm, the diminution in the area of hepatic flatness and the movable abdominal dullness made it reasonably certain that a perforation had occurred. Dr.

Mitchell saw the patient shortly after 12 midnight and agreed that an operation was advisable. The operation was performed about 8 hours after the time at which perforation had occurred.

Healed Amoebic Abscess of the Liver, and Amoebic Abscess of the Lung. Exhibitions of Specimens. DR. OPIE.

The patient was admitted to the hospital March 1, 1900, complaining of pain in the right side and shoulder. He had had dysentery for 13 months but it had disappeared three months before his admission. For about six months he had had pain in the right side and in the right shoulder. When admitted he was emaciated and pale and his skin had a yellowish hue. There was bulging of the lower portion of the right chest below the level of the 5th rib and distention of the abdomen on the right side below the costal margin. The dullness began at the 5th rib in the mammary line, at the 6th rib in the mid-axillary line and at the 8th rib in the line of the angle of the scapula; it extended about 8.5 cm. below the costal margin in the right mammary line. Several exploratory punctures were made but the bloody fluid obtained contained no amœbæ. There was no diarrhœa and amœbæ were not found in the stools.

An operation was performed by Dr. Cushing seven days after admission. The 10th rib was resected in the mid-axillary line and a large abscess cavity entered. It contained about a litre of chocolate-colored fluid in which were necrotic particles. The discharge after the operation was profuse, and in it on the second day actively motile amœbæ were found. The cavity was irrigated with quinine solution varying in strength from 1 to 1000 to 1 to 3000. The discharge gradually diminished in amount and at the end of six weeks had completely disappeared. Amœbæ were frequently found during this period.

On the 5th day after the operation the patient was attacked with cough, which gradually increased in severity and was accompanied by the expectoration of mucopurulent material. At first nothing specific was found in this material but later actively motile amœbæ were discovered. As the cough became worse signs of consolidation appeared over the lower right chest. Eight weeks after the first operation the rib was resected in the anterior axillary line but no abscess cavity was found. A second incision made through the 5th rib at the juncture of the costo-chondral line entered an abscess cavity from which was evacuated a large amount of purulent fluid. The material discharged from this cavity contained numerous amœbæ. On the 4th day after operation occurred a profuse hæmorrhage, with which about a pint and a half of blood was lost. A second hæmorrhage took place eight days later and death followed.

The case was one of dysentery followed by an amœbic abscess of the liver. The dysentery was presumably of the same character though amœbæ were not found in the stools. Following operation the liver abscess healed but death followed the formation of a secondary abscess in the lung.

At autopsy was found in the right lung the large abscess

cavity which is well seen in the preserved specimen. The pleura was adherent to the chest wall and the abscess cavity occupied almost the entire anterior half of the middle and lower lobes. The walls are irregular and covered with a soft necrotic material. In the liver, the abscess cavity which two months before death contained a litre of purulent fluid is represented by a small mass of dense fibrous tissue 3 cm. across. In the ascending colon and in the cœcum were numerous pigmented scars, while in the sigmoid flexure were one or two very superficial ulcers. In the contents of the lung cavity were numerous motile amœbæ. None could be found in material scraped from the intestinal ulcers, though it can be hardly doubted that amœbæ were present during the active stage of the dysentery.

The etiological relationship of amœbæ to so-called amœbic dysentery is not entirely undisputed. The presence of amœbæ in the walls of abscesses in organs distant from the infected intestines furnishes the best evidence of their pathogenicity. The amœbæ are constantly associated with one form of dysentery characterized by the occurrence in the large intestine of a lesion whose distinctive feature is necrosis and softening of the submucous tissue with the production of irregular ulcers with undermined edges. That they are the causal factors in the production of the disease has been questioned since on the one hand a variety of bacteria are always present and on the other hand similar amœbæ have been found by Cunningham, Grassi, Sehuberg and others in the stools of healthy individuals and of those suffering with other diarrhœal diseases.

Belief in the pathogenicity of the *Amœba eoli* is justified by certain facts: (1) Amœbæ are constantly associated with a form of dysentery which is characterized by peculiar anatomical lesions; they occur within the lesions and in the discharges from them. (2) They are found in abscesses of the liver and of the lung accompanying this form of dysentery but are not found in other abscesses of these organs. (3) Though the anatomical picture of chronic tropical dysentery has not been reproduced in animals, an inflammatory condition of the large intestine accompanied by multiplication of the organism in the lumen of the intestine and in the affected tissue has been produced (Kruse and Pasquale) by injecting into the rectum of cats purulent material from liver abscess containing only amœbæ. The injection of non-dysenteric faecal material containing amœbæ has not caused a similar condition.

Exhibition of a Case of Osteoma of External Auditory Canal. DR. RANDOLPH.

It is seldom we have the opportunity of seeing new growths in the external auditory canal. The most common one is an osteoma, which occurs either as a localized exostosis or as a more diffuse hyperostosis, the etiology of which is rather obscure. Buek, of New York, thinks that they are often due to the irritation produced by a chronic discharge. I doubt very much whether this is the true interpretation of it. We know how frequently otorrhœa is seen and how seldom we meet with an exostosis.

The treatment does not call for aggressive measures except in a very limited number of cases. If the patient is quite deaf in one ear and an osteoma is interfering with the better ear, then an operation should be undertaken. Or if there is a discharge from that ear the tumor should be removed lest its growth should close the orifice and cause serious symptoms. Otherwise the tumor is allowed to stay. When it completely fills the canal its development seems to come to a standstill and it gives no further trouble than to interfere with hearing. The great trouble about operative measures in these cases is that it is very difficult to remove the tumor without running some risk of producing inflammation which may extend to the drum membrane and produce a more serious condition. Last year I made mention, in my report in "Progressive Medicine," of the only other case I have seen and upon which I operated successfully. The man was quite deaf in one ear and the osteoma was attached to the superior wall, and apparently filled the whole external auditory canal nearly to the drum membrane. I perforated the growth by applying to it nitrate of silver fused on the end of a probe and applying it at long intervals until I had gotten clean through the growth. It produced such a disturbance in the nutrition of the growth that it was easily broken down and in 3 months' time the canal was entirely clear. This seems a long and rather tedious treatment to adopt but it was attended with no irritative symptoms and was followed with complete success.

This boy's osteoma fills up the canal entirely but I have not suggested any operation here, because it does not seem to be called for.

Suspension of the Kidney. An Extensive Vesico-Vaginal Fistula.

DR. KELLY.

(To appear later.)

February 4, 1901.

Exhibition of Medical Cases. Chronic Jaundice with Xanthoma Multiplex. DR. OSLER.

The patient, aged 39, had typhoid fever with cholelithiasis in 1897 and has had three attacks of biliary colic (the first in December, 1899), characterized by pain, vomiting, chills, fever, sweats and jaundice, and following each attack the jaundice has deepened. The form of jaundice is that associated with stone in the common duct, that is to say, intermittent in character and deepening after the attacks of colic, etc. The unusual complication is the presence of what is known as Xanthoma multiplex.

All of you have noticed, especially in brunettes, a distinct little tumor on the eyelids, sometimes on both but usually on the lower lid, the common Xanthelasma palpebrarum. In a few rare instances these remarkable tumors are widely distributed over the body, usually in connection with chronic jaundice. Oddly enough Dr. Sabin a day or two ago met another patient with the same condition in chronic jaundice.

In a few rare instances multiple Xanthelomata have occurred in young persons without jaundice. Not only do the

tumors occur in the skin but in a few cases in the mucous membranes, on the serous surfaces and in the bile passages, the gall-duct and gall-bladder. In this patient the distribution is on the hands, elbows, axillæ, neck and on the toes; they are chiefly in the folds and at points of irritation.

The yellow color is due to the presence of supposed characteristic cells sometimes spoken of Xantheloma cells, which undergo a fatty degeneration and the color is due to the fat. Occasionally these tumors undergo complete involution and thus disappear. This patient will have an operation performed for removal of the gall-stone and it is to be hoped the tumors will disappear, but in any case they are never serious, do not grow very large and are a source of annoyance only through the slight disfigurement produced. She has one patch on the mucous membrane of the upper lip but there are only a few small ones about the eyelids.

DISCUSSION.

DR. WELCH.—I hope that a careful histological study will be made of specimens of the xanthomatous lesions in this case, as the subject is one offering many unsolved problems. My attention was directed a few years ago to Xanthoma through the opportunity of examining sections sent to me by Dr. Pollitzer of New York, whose specimens were utilized by Unna in his description of generalized Xanthoma. The specimens which I examined were of ordinary Xanthoma palpebrarum. There appear to be at least three, and probably more, clinical types of disease which have been called Xanthelasma or Xanthoma, namely, Xanthoma vulgare of the eyelids, an extremely common and unimportant affection, juvenile Xanthoma multiplex, and generalized Xanthoma of adults, most frequently secondary to jaundice and diabetes mellitus, but occurring also without any apparent cause. Unna makes a sharp histological difference between the common form of palpebral Xanthoma and generalized Xanthoma. According to him, in the former the fat, which gives the yellow color to the lesion, is of a peculiar character and lies in extracellular masses within the lymphatic spaces and vessels, there being no true Xanthoma cells. I am not aware that Unna's views, which are not in accordance with those usually accepted, have been confirmed. Waldeyer in his first publication and most other investigators following him find the fat in small granules or droplets within large cells believed to be derived from connective-tissue cells or endothelial cells, these fatty cells being the so-called Xanthoma cells. Later Waldeyer suggested that these cells may come from his plasma cells or Toldt's embryonic fat-forming cells, and this view has had a number of advocates. Dr. Pollitzer finds evidence in his sections of palpebral Xanthoma that the characteristic cells containing fat are derived from striped muscle, partly displaced through congenital abnormality into the corium. Virchow objects to the designation "Xanthelasma" or "Xanthoma," as not based upon histological characters, and has proposed, as a substitute, fibroma lipomatodes, but this suggestion seems to have met with little success. There is a

rare form of lipoma which bears considerable anatomical resemblance to certain of the larger neoplasms which have been described as Xanthomata. I examined such a specimen some years ago. It was a lobulated and encapsulated subcutaneous tumor, the size of a hen's egg, removed from the groin of a young man, and believed at the operation to be an ordinary lipoma. On section it presented a uniform, yellow surface, and microscopically it was composed entirely of vascular stroma and large cells filled with minute granules or droplets of fat. After removal of the fat single, or occasionally multiple, round or oval nuclei with nucleoli were found usually about the middle of cells filled with a finely porous or reticulated protoplasm. There was a stroma around individual cells or groups of cells. I interpreted the tumor as composed of embryonic adipose tissue. There were no adult adipose-tissue cells with single, large oil-drops. I mention this tumor on account of its histological resemblance to certain xanthomatous tumors, but otherwise it has no relation to Xanthoma, as it was the only new growth and was in the subcutaneous tissue. It is highly probable that a variety of distinct affections have been described under the name of Xanthoma.

A Case of Arsenical Neuritis. DR. SABIN.

The patient is a young woman who was brought to the hospital two months ago, November 23, 1900, after having taken about a dram of Rough on Rats. She came in a few hours later saying she had felt well for two hours after taking the poison but had then begun to vomit. Her stomach was washed out repeatedly and large doses of the antidote given, together with epsom salts and castor oil. The only troublesome symptoms she exhibited while in the hospital were nausea and vomiting. She was dismissed in five days feeling well, but noted that on walking up the steps of her home her feet were numb and the steps felt soft. She was soon able to be up and about but the numbness of the feet never left her. On January 1 she had an attack of painful micturition that was followed by fever lasting six days. The numbness of the feet gradually increased and she became unable to walk.

When she came to the hospital again she had double foot-drop and wrist-drop, the muscles involved, however, were not entirely paralyzed. Her hands were so weak that she could not feed herself. Electrical reaction was given only with strong currents. There was delayed sensation over the legs and arms, and slight impairment in the fingers and toes but no complete anaesthesia. There was hyperaesthesia of the soles of the feet so that the slightest touch caused pain and muscle spasm. When she came in there was some keratosis over the soles of the feet. The palms of the hands were not thickened but since admission some keratosis has developed. The skin is everywhere dry and scaly. On both hands there is a white line running transversely across each nail. The skin reflexes are increased, the deep reflexes absent.

DISCUSSION.

DR. OSLER.—It is interesting that neuritis seen in general practice occurs in persons who have taken a considerable quantity of arsenic at one time and not in those who take a large quantity over a prolonged period. Arsenic is one of the medicines most commonly used, and yet we rarely see a neuritis following it. We have had but one case before in the hospital and that patient took one ounce and two drachms of Fowler's solution. There has been in the city a case (seen by Dr. Carey Gamble in consultation) of fatal neuritis following the use of arsenic for chorea. Arsenic is a drug that may be taken in considerable doses for long periods without any damage whatever, and the cases of neuritis that do occur are probably in patients who have an idiosyncrasy for it. Hutchinson reports a case of a man who had taken arsenic nearly all of his life and without showing even pigmentation.

A Case of Pemphigus Vegetans. DR. HAMBURGER.

(To appear, with discussion, later.)

The Frequency of Typhoid Bacilli in the Blood. DR. COLE.

(See page 203.)

SUMMARIES OR TITLES OF PAPERS BY MEMBERS OF THE HOSPITAL AND MEDICAL SCHOOL STAFF APPEARING ELSEWHERE THAN IN THE BULLETIN.

CHARLES RUSSELL BARDEEN, M. D. The Function of the Brain in *Planaria Maculata*.—*American Journal of Physiology*, Vol. V, No. 3.

— and ARTHUR WELLS ELTING, M. D. A Statistical Study of Variations in the Formation and Position of the Lumbo-sacral Plexus in Man.—*Anatomischer Anzeiger*, Bd. 19, Nos. 5-6.

LEWELLYS F. BARKER, M. D. On the Importance of Pathological and Bacteriological Laboratories in connection

with Hospitals for the Insane.—*Indiana Medical Journal*, January, 1901; *The American Journal of Insanity*, January, 1901.

— The So-called Cardiac Neuroses: Classification; Etiology; Pathology.—*Chicago Medical Recorder*, May, 1901.

E. BATES BLOCK, M. D. Enchondroma-like Formations in the Femur, following Osteomyelitis.—*Journal of Pathology and Bacteriology*, February, 1901.

JOSEPH C. BLOODGOOD, M. D. Blood Examinations as an Aid to Surgical Diagnosis.—*American Medicine*, May 18, 1901.

THOMAS R. BROWN, M. D. A Review of Some of the Recent Work on the Physiology and Pathology of the Blood.—*Maryland Medical Journal*, December, 1900; February, March, April, May, 1901.

——— The Prospect in the Treatment of Lobar Pneumonia.—*Maryland Medical Journal*, January, 1901.

——— Urinary Hyperacidity: A Consideration of Cases with Symptoms Suggestive of Cystitis, but with no Infection, Due to this Cause.—*Philadelphia Medical Journal*, March 2, 1901.

——— Notes on the Blood and Vesicle Cells in Dr. Smith's Case of Epidermolysis Bullosa.—*Maryland Medical Journal*, April, 1901.

——— On the Relation Between the Variety of Micro-Organisms and the Composition of Stone in Calculous Pyelonephritis.—*Journal of the American Medical Association*, May 18, 1901.

THOMAS S. CULLEN, M. D. The Cause of Cancer.—*American Medicine*, May 18, 1901.

HARVEY CUSHING, M. D. Concerning Prompt Surgical Intervention for Intestinal Perforation in Typhoid Fever, with the Relation of a Case.—*Annals of Surgery*, May, 1901.

——— and BRUCE W. GOLDSBOROUGH, M. D. A Rare Form of Extrauterine Pregnancy.—*American Medicine*, April 6, 1901.

——— Sur la Laparotomie Explorative Précoce dans la Perforation Intestinale au Cours de la Fièvre Typhoïde.—*Archives Générales de Médecine*, January, 1901.

SIMON FLEXNER, M. D. Experimental Pancreatitis.—*University Medical Magazine*, January, 1901.

——— Etiology of Dysentery.—*The Journal of the American Medical Association*, January 5, 1901.

——— The Etiology of Tropical Dysentery.—*Centralblatt für Bakteriologie*, Erste Abt., Bd. 28, No. 19.

WILLIAM W. FORD, M. D. Variation of the Properties of the Colon Bacillus, Isolated from Man.—*Journal of the Boston Society of Medical Sciences*, January 15, 1901.

——— Obstructive Biliary Cirrhosis.—*American Journal of the Medical Sciences*, January, 1901.

——— On the Bacteriology of Normal Organs.—*The Journal of Hygiene*, Vol. 1, No. 2.

THOMAS B. FUTCHER, M. D. Syphilitic Fever, with a Report of Three Cases. (From the Service of Professor William Osler.)—*New York Medical Journal*, June 22, 1901.

NORMAN B. GWYN, M. D. The Disinfection of Infected Typhoid Urines.—*Proceedings of the Phila. County Medical Society*, Vol. XXI, No. 7; *Philadelphia Medical Journal*, January 12, 1901.

NORMAN HARRIS, M. D. A Preliminary Report upon a Hitherto Undescribed Pathogenic Anaërobic Bacillus.—*Journal of the Boston Society of Medical Sciences*, February 19, 1901.

ROSS GRANVILLE HARRISON, M. D. Ueber die Histogenese des peripheren Nervensystems bei *Salmo salar*.—*Archiv für Mikroskopische Anatomie*, Bd. 57, Heft 2.

ALBION WALTER HEWLETT, M. D. The Superficial Glands of the Oesophagus.—*The Journal of Experimental Medicine*, Vol. V, No. 4.

HENRY BARTON JACOBS, M. D. A Short Account of the Recent International Medical Congress in Paris.—*The Boston Medical and Surgical Journal*, January 10, 1901.

——— Four Cases of Sporadic Cretinism.—*Maryland Medical Journal*, March, 1901.

HOWARD A. KELLY, M. D. Jules Lemaire. The First to Recognize the True Nature of Wound Infection and Inflammation, and the First to Use Carbolic Acid in Medicine and Surgery.—*Journal of the American Medical Association*, April 20, 1901.

——— How to Deal With the Vermiform Appendix: Some Forms of Complicated Appendicitis.—*American Medicine*, April 20, 1901.

THOMAS McCRAE, M. D. Abdominal Pain in Typhoid Fever.—*New York Medical Journal*, May 4, 1901.

G. BROWN MILLER, M. D. The Streptococcus Pyogenes in Gynecologic Diseases.—*Journal of the American Medical Association*, May 18, 1901.

M. ADELAIDE NUTTING. The Preliminary Education of Nurses.—*The American Journal of Nursing*, March, 1901.

EUGENE L. OPIE, M. D. The Relation of Cholelithiasis to Disease of the Pancreas and to Fat Necrosis.—*American Journal of the Medical Sciences*, January, 1901.

—— On the Relation of Chronic Interstitial Pancreatitis to the Islands of Langerhans and to Diabetes Mellitus.—*The Journal of Experimental Medicine*, Vol. V, No. 4.

—— The Relation of Diabetes Mellitus to Lesions of the Pancreas. Hyaline Degeneration of the Islands of Langerhans.—*The Journal of Experimental Medicine*, Vol. V, No. 5.

WILLIAM OSLER, M. D. On Perforation and Perforative Peritonitis in Typhoid Fever.—*Proceedings of the Philadelphia County Medical Society*, January, 1901, and *Philadelphia Medical Journal*, January 19, 1901.

—— A Plea for the More Careful Study of the Symptoms of Perforation in Typhoid Fever with a View to Early Operation.—*The Lancet*, February 9, 1901.

—— The Medical Aspects of Carcinoma of the Breast, with a Note on the Spontaneous Disappearance of Secondary Growths.—*American Medicine*, April 6 and 13, 1901.

—— Hemorrhage in Chronic Jaundice.—*American Medicine*, April 27, 1901.

—— The Study of Internal Medicine.—*Medical News*, April 27, 1901.

—— The Natural Method of Teaching the Subject of Medicine.—*The Journal of the American Medical Association*, June 15, 1901.

LINDSAY PETERS, M. D. Resection of the Pendulous, Fat Abdominal Wall in Cases of Extreme Obesity.—*Annals of Surgery*, March, 1901.

HENRY O. REIK, M. D. The Value of Formaldehyde in the Treatment of Suppurative Otitis Media.—*Maryland Medical Journal*, January, 1901.

HUNTER ROBB, M. D. The Treatment of Nausea and Vomiting Following Anaesthesia after Abdominal Operations.—*Cleveland Medical Gazette*, February, 1901.

B. R. SCHENCK, M. D. Four Cases of Calculi Impacted in the Ureter. Nephro-Ureterectomy, Abdominal Uretero-Lithotomy, Vaginal Uretero-Lithotomy.—*Journal of the American Medical Association*, May 11, 1901.

WALTER R. STEINER, M. D. Dermatomyosites, with Report of a Case which also Presented a Rare Muscle Anomaly, but Once Described in Man. (Abstract.)—*Journal of the Boston Society of Medical Sciences*, February 19, 1901.

SAMUEL THEOBALD, M. D. The Evolution of the Ophthalmoscope and what it has done for Medicine.—*New York Medical Journal*, June 22, 1901.

GEORGE WALKER, M. D. Curetting the Urethra in the Treatment of Chronic Posterior Urethritis.—*Maryland Medical Journal*, March, 1901.

—— Tuberculosis of the Vesiculæ Seminales, Testes and Prostate; Complete Exeision of Right Side; Incision and Curetting on Left Side: Cured.—*Maryland Medical Journal*, February, 1901.

WILLIAM H. WELCH, M. D. Distribution of Bacillus Aerogenes Capsulatus. (Bacillus Welchii, Migula.)—*Journal of the Boston Society of Medical Sciences*, February 19, 1901.

HUGH H. YOUNG, M. D. An Operating Table for Office Work.—*Maryland Medical Journal*, March, 1901.

—— Ueber ein neues Verfahren zur Exstirpation der Samenblasen und der Vasa deferentia, nebst Bericht über zwei Fälle.—*Archiv für klinische Chirurgie*, Bd. 62, Heft 3.

NOTES ON NEW BOOKS.

Golden Rules of Surgical Practice. By E. HURRY FENWICK, F. R. C. S. Golden Rules Series, No. I. Fifth edition. Revised and enlarged. (Bristol: John Wright & Co.)

Golden Rules of Obstetric Practice. By W. E. FOTHERGILL, M. A., B. Sc., M. D. Golden Rules Series, No. III. (Bristol: John Wright & Co.)

Golden Rules of Physiology. By I. WALKER HALE, M. B., Ch. B. (Vict.), and J. ACWORTH MENZIES, M. D., C. M. (Ed.). Golden Rules Series, No. VI. (Bristol: John Wright & Co.)

Golden Rules of Ophthalmic Practice. By GUSTAVUS HART-
RIDGE, F. R. C. S. Golden Rules Series, No. VII. (Bristol: John Wright & Co.)

These little books have been published to aid students in preparing for examinations, and, as one would naturally suppose, they combine a maximum of information with a minimum of space. Their size in fact suggests that they are intended to be pocket-guides and private lights until the shoals and reefs of an examination are safely passed. If guides are required in cramming for an examination, these seem to be exceptionally well written and printed, and can be commended.

Essentials of Histology. By LOUIS LEROY, M. D. 72 illustrations. (Philadelphia: W. B. Saunders & Co., 1900.) Price, \$1.

This small volume is a quiz compend with very diagrammatic illustrations. It may afford solace to those contending against the rigor of State Board examinations; but to the sincere student of anatomy it is of little interest.

A Text-Book upon the Pathogenic Bacteria, for Students of Medicine and Physicians. By JOSEPH MCFARLAND, M. D. Third edition. (Philadelphia: W. B. Saunders & Co., 1900.)

The second edition of this work was reviewed in the Bulletin of December, 1898.

We ask the attention of our readers to the vast improvement made in this, the third edition, compared with that of its pre-

deceases; inaccuracies have been corrected, chapters carefully rewritten, and much new and valuable material introduced.

Especially to be commended are the chapters upon Infection and Immunity, which are made to embrace the latest views of the various well-known authorities in these speculative fields of research; the articles upon Tuberculosis, Diphtheria, Typhoid Fever and Plague; whilst the chapters dealing with general technique have undergone satisfactory revision.

Dr. McFarland is to be congratulated upon the excellent merit of this volume. N. MACL. H.

An American Text-book of Physiology. Edited by WILLIAM M. HOWELL, Ph. D., M. D. Second edition, revised. Vol. II. (Philadelphia: W. B. Saunders & Co., 1901.)

The second edition of the American Text-book of Physiology, edited by Professor Howell, has recently been completed by the appearance of its second volume. The first volume of this edition was placed before the public some time ago and was reviewed in the February number of the BULLETIN. Most of the opinions there expressed relating to the value of the work in general might be repeated here, but such a repetition is considered unnecessary.

The second volume treats of the general physiology of muscle and nerve, the central nervous system, the special senses, of special muscular mechanisms, and of reproduction. The authors who contributed to the first edition have rewritten their respective subjects for this volume.

Professor Lombard's article on the general physiology of muscle and nerve contains very much valuable knowledge, knowledge that is especially interesting to the advanced student in physiology. This is probably explained in part by the fact that a very large amount of detail is introduced. But it is just this that detracts, to some extent, from its value to the beginner. In the treatment of such subjects as the spread of electrostatic charges, the effect of temperature upon the irritability of nerve and muscle, contraction in normal muscle following frequent excitation, etc., the detail is almost sufficient to overwhelm the average student. At the same time the brevity that the character of the article necessitates leads to an inevitable lack of clearness. The brief and incomplete reference to v. Furth's work on the proteids of muscle will convey to the student but a vague idea of its meaning in the chemical and physiological processes of muscle. On the other hand it is noticeable that the article has been carefully brought up to date. Practically all of the recent important work receives notice. The rather vague statement of the neuron theory in the first edition gives place to a clear and definite exposition in the present volume. The additions to our knowledge of the physiological processes in muscle made through physical chemistry are referred to. The work of Bottazzi, Bonettan, Budgett, v. Furth, and many others has been incorporated in the text. In this connection we must say that Lombard has added an interpretation to the work of Budgett and Green which these authors do not mention. Lombard is discussing the question, do nerve fibres conduct the impulse in both directions from the point of stimulation? It will be remembered that Budgett and Green cut the pneumogastric nerve between the ganglion and the cranium, and then sutured its peripheral cut end to the peripheral cut end of the hypoglossal. Three months after operation stimulation of the central end of the vagus caused the muscles of the tongue to contract. "... There would seem to be no escape from the conclusion that the sensory fibres of the pneumogastric had conducted the impulse centripetally as far as the ganglion and then centrifugally down to the muscles of the tongue." This is true, but in so doing the nerve fibres were conducting in the direction in which they normally conduct—

first to the nerve cell, then from the nerve cell. At no time was the impulse carried in a direction opposite to its normal one. The experiment does not demonstrate the power of nerve fibres to conduct in both directions.

The article on the central nervous system by Professor Donaldson has been rearranged and largely rewritten so as to render this subject more "suitable to the needs of students and practitioners." In a brief introduction generalizations are expressed with a degree of simplicity and clearness that is charming. As a general rule these attractive qualities of style are maintained throughout the article. It is to be regretted that the author has permitted to appear in the text his categorical descriptions of the cranial nerves. It is true that the student is referred to Barker's work on the nervous system for more complete descriptions; still the insertion of a diagram, especially of the cochlear nerve, or a more definite statement of the relations of the various parts, might have made such reference unnecessary. We believe that some improvement could still be made in the way of rendering the work more useful to medical students. Thus the treatment of aphasia, a subject of considerable interest in itself and besides of some clinical importance, is rather brief, while to the growth of the brain probably more space is devoted than its importance to the medical student calls for. The subject is carefully brought up to date by the addition of most of the recent work, such as that of Nissl and Marinesco. A large amount of material has been drawn from Barker's compendium, "The Nervous System and its Constituent Neurons."

Professor Bowditch's article on the sense of vision is practically unchanged. The only real additions made are included in the two paragraphs which embody the views of Müller on color perception and Einthoven's explanation of the illusion of space-perception. The author takes advantage of the new edition to insert many references that were omitted in the first edition. These might be still further improved by the addition of dates. As far as style, appropriate selection, and coordinate treatment are concerned, there is nothing that could be wished for.

The articles on the remainder of the "special senses," in which are apparently included the senses of hunger, thirst and equilibrium, are contributed by Professor Sewall. With the exception of slight alterations in the articles on hearing, cutaneous and muscular sensations and equilibrium necessary to bring them up to date, these articles stand as they were in the first edition. The anatomical expositions are excellent, the style clear, and the subject-matter as complete as the limitations of a text-book permit.

The fact that under the physiology of the "Special Muscular Mechanisms" only the physiology of locomotion and of the voice and speech are developed, might influence the beginner into believing that these are the only special muscular mechanisms. A brief reference to the special mechanisms treated in other parts of the work might have freed it from this ambiguity. The articles under this head by Lombard and Sewall call for no special comment.

The fascinating article of Lee on reproduction has been kept up to its original high plane by the addition of the recent literature. Thus Schenk's views on the determination of sex receive an appropriate notice, and Arrhenius' interesting suggestion that the rhythmicity of menstruation might possibly be dependent upon synchronous variations in atmospheric electricity is referred to. A few loose statements from the first edition have crept into the second, *e. g.*, "the thickness of the spermatozoan is .055 mm.," "the number of chromosomes in the chromatin," "the most abundant of the solid chemical constituents of the spermatozoan is nuclein, probably in the form of nucleic acid."

So much for the text-book so far as the individual contributors are concerned. The advantages and disadvantages of a text-book written by a number of authors are obvious and have been fully and frequently discussed. The advantages in this special case have been well brought out in the review of the first volume of this text-book above referred to. One of the disadvantages (arrangement) was also then mentioned. Beside disadvantageous arrangement, omission is quite apt to occur. Every attempt has apparently been made to guard against this in the work under consideration. The only omission of any importance that the reviewer has discovered is a treatment of the knee-jerk phenomenon. Donaldson, in speaking of nervous background, mentions reinforcement of the knee-jerk, apparently taking it for granted that this subject has been treated by Lombard. Lombard, however, says nothing about it, probably believing that it does not come within his sphere. The text-book is thus minus a discussion of this important phenomenon, which is so much the more to be regretted when we recall the fact that one of the contributors (Lombard) has devoted so much of his time to the investigation of this very point.

It is to be distinctly understood that the unfavorable criticisms herein mentioned involve only minor points which may be found in every text-book if looked for. Indeed one is struck by their relative infrequency in the book under discussion. And after a thorough perusal of the American Text-book of Physiology the reviewer believes, as has been stated by another elsewhere, that "on the whole this work is certainly the best text-book of physiology for medical students in the English language, and it will doubtless continue to be used generally in all medical schools of the first class."

J. E.

A Medico-Legal Manual. By WILLIAM W. KEYSER, Lecturer on Medical Jurisprudence and Judge of the District Court, Omaha. (Omaha: Burkley Printing Co., 1901.)

This excellent little book has been written by the author for the benefit of physicians and aims to present the legal side of medical jurisprudence. It gives legal terms and principles with the laudable purpose of preparing the medical man to acquit himself creditably as an expert witness.

The author takes a most sensible view of the vexed question of expert testimony. He says: "Much of the odium heaped on opinion-evidence is chargeable to present methods of selecting expert witnesses. Each side calls only those whose opinions are preascertained and favorable. The witnesses are biased by a desire for victory for the side which enlists them, particularly so if the opposing experts are members of other schools of practice. Justice is thwarted, advance in medical science is retarded and the profession is disgraced. It is not the province of this work to advocate any particular method of procuring expert testimony; but it is proper to urge the professions of law and medicine to extricate this valuable branch of evidence from its humiliating situation. Expert witnesses should be called by the State or by the trial judges, not as friends or supporters of either side, but as advisers of the court. Their fees should be paid out of a general fund and should not depend on the result of the case. Indeed, so far as may be, they should occupy a position as independent and impartial as that of the judge or jury."

The chapter entitled "The Doctor as a Witness" is eminently clear, practical and marked by good sense. It should be read by every young physician.

The book as a whole is worthy of all praise. It is a manual and not an exhaustive treatise, and cannot supersede the classical works on jurisprudence.

Golden Rules of Skin Practice. By DAVID WALSH, M. D., Edinburgh. Golden Rule Series, No. VIII. pp. 102. (Bristol: John Wright & Co., 1900.)

A tersely written and convenient little manual for the treatment of diseases of the skin. The directions given for the use of remedies are sensible and judicious.

Urinary Diagnosis and Treatment. By J. W. WAINWRIGHT, M. D. (Chicago: G. P. Engelhard & Co., 1900.)

In this small work of 134 pages, the author attempts to give the simplest methods of urine examination with the most recent ideas concerning the treatment of urinary disorders. As he states that he wishes to avoid the more or less elaborate accounts of larger books, it is probably not proper to offer any criticism as to his descriptions except on one important point, namely, clearness. The shorter such things are made the more necessary for the absence of any doubt as to what is meant. For example, the writer lays much stress on the recognition of the number and kind of casts, and yet his description of them is at times even puzzling. Thus one might have some difficulty in knowing what was meant by this: "If the epithelium be attached to the tube and is discharged alone and after the epithelial cast, we have the *hyaline casts*."

The busy general practitioner, for whom the work is intended, would be better to consult a more elaborate manual for his urinary work. The prescriptions, formulæ of solutions and tables along with the plates, which are from Hoffman and Ultzmann, will all be found useful. These, with the occasional notes on treatment, are the best features of the book.

The American Year-book of Medicine and Surgery for 1901. In two volumes. Vol. I. General Medicine. Vol. II. General Surgery. (Philadelphia and London: W. B. Saunders & Co., 1901.)

The division of this work into two volumes, which was begun last year, has proved so satisfactory that it is continued. The smaller volumes are much more easily handled. There is little to be said of the Year-book except to repeat our previous commendation of it. It has been found most useful and reliable. When one considers the possibility of error in the handling of so many references, the care taken in the preparation of the articles must be evident. The Year-book is worthy of the support of the profession. Dr. Gould and his contributors are to be congratulated on the volumes for this year.

The Tale of a Field Hospital. By FREDERICK TREVES. (London and New York: Cassell & Co., 1900.)

We have long known with what a graphic pen Mr. Treves can write of disease and its manifestations. He has shown in the present work that he can equally well describe places and events. This is a small volume, very neatly gotten up and illustrated by excellent photographs. It gives the account of the field hospital with Buller's force, with which Mr. Treves was connected. The chapters show the clear-cut description which has been such a feature of the recent work of war-correspondents. The text is not specially professional in tone, there are no technical descriptions, and yet throughout one feels that the eyes by the help of which we see are those of one of our own profession.

It is impossible to quote much of the contents. The sombre note must predominate in the account of a field-hospital. Perhaps the chapter on "The Two White Lights" is the best example of this. The situation of the hospital was marked at night by two white lights on a flagstaff, and one can imagine what the sight of them meant to the wounded who were being brought in. The query of the wounded man in the bottom of

the ambulance sums it up: "Don't you see nothing yet, Bill, of the two white lights?" The other side is not lacking, as is shown in the chapter on "The Body-snatchers." This name was given to a volunteer ambulance corps of two thousand men recruited from everywhere but who seem to have done excellent service. They became the butt of many jokes and were known as "body-snatchers," "catch-em-alive-ohs" or the "pick-me-ups." The constant habit of the "tommies" is to turn everything into a jest.

Mr. Treves has paid close attention to the feelings and sentiments of the common soldiers. He bears testimony everywhere to his courage and patient endurance. Little is said in reference to the hospital management, yet one gathers that the author considers the best possible to have been done.

The Medical Annual. A Year-book of Treatment and Practitioner's Index. (1901. Bristol: John Wright & Co.; New York: E. B. Treat & Co.; Toronto: J. A. Cawell & Co.)

This is the nineteenth year of this annual and the standard of previous years is well kept up in the present volume. There are now seven contributors from this side of the Atlantic. The title explains the purpose of the book. It is divided into sections, of which the first deals with the new remedies of the year. The author in his introduction alludes to the decline in the art of prescribing and quotes the remark that "with some practitioners the atrophy of disuse has almost blighted their capacity to think out and indite a good prescription." We would rather suppose that in many of the younger generation such a capacity has never existed. There is a good article on toxins and anti-toxins in this section. By far the greater part of the book is taken up with the discussion of new treatment. Subjects are taken up alphabetically, the principal articles on the subject are extracted and the list of references given. It is impossible to review such numerous articles, but those on the digestive system and heart seem especially good. Throughout, however, the work has been well done. The third section includes sanitary science, recent legal decisions of interest in medicine, a review of new inventions and appliances, and a list of the new books of the year, medical journals, etc. This volume can be recommended as previous ones to be of much use, especially to the busy practitioner.

Tropical Diseases. A Manual of the Diseases of Warm Climates. By PATRICK MANSON, M. D., LL. D. (London and New York: Cassell & Co., 1900.)

This is a revised edition of this work, which has now grown to nearly 700 pages. The small size renders it very convenient for carrying, a point kept in view in the preparation of the volume. The book opens with the consideration of malaria, to which considerable space is given. The part played by the mosquito is fully described and illustrated by diagrams. The discussion of the disease is thorough as might have been expected. The section on haemoglobinuric fever is especially interesting. Yellow fever, Bubonic plague and various rarer diseases are next considered. The account of beriberi is given in a graphic way, and the description of the disease is excellent. In taking up dysentery, Dr. Manson points to the probability of what has more recently been practically established in regard to the various factors in the causation of the disease. Abscess of the liver is discussed at some length. Perhaps the most interesting section is that on animal parasites and associated diseases. Regarding filiaris especially, Dr. Manson is well qualified to speak, and this is a most valuable portion of the work.

There are few works on medicine that can be read with more pleasure in addition to profit than this one. One reads not only for the interest of the subject, but also for the style of the

writing. It is to be regretted that this is not a characteristic of more medical works.

A Pilgrimage; or the Sunshine and Shadows of the Physician. By WM. LANE LOWDER, B. S., M. D. (Louisville, Ky.: R. H. Carothers.)

This little volume is the outgrowth of a series of essays read before several county medical societies in Kentucky. The intention of the book is to dignify and ennoble the profession of medicine. The sentiments contained in it are unexceptionable but commonplace. They are enforced by trite quotations from familiar poets, living and dead. The following from the first page will serve as an example of the one hundred and ninety pages which follow:

"The career of the physician begins with his determination to study medicine and terminates with his death; or, as is so beautifully portrayed by the immortal Gray in that matchless poem 'The Rude Forefathers of the Hamlet,' when

'The breezy call of incense breathing morn,
The swallows twittering from the straw-built shed,
The cock's shrill clarion or the echoing horn
No more shall rouse them from their lowly bed.'

Then it is, and not till then, that his labors cease and his trials are all ended. The morning of this life should be commenced with aseptic hands and a sterilized heart, that the ambition to realize the ideal in a profession, honored in all ages by all men, will not be infected by skepticism or greed."

If one has time to read these excellent but thread-bare sentiments he will surely receive no damage. The question, however, obtrudes itself whether it is worth while for the author to spend "the dark and silent hours of the night—hours stolen from sleep; hours usually allotted to the repose of body and mind"—in writing them, as we are assured he has. The purpose of the book is good.

Nursing Ethics for Hospital and Private Use. By ISABEL HAMPTON ROBB. (Cleveland: J. B. Savage, 90-92 Wood Street, 1901.)

While books on the subject of nursing are rapidly increasing in number and variety, this is the first attempt in this country, so far as we know, to deal with this subject from any but the practical and technical standpoint. In the twelve chapters of which the book is composed we find first the subject of nursing as a profession thoroughly discussed, and supplemented by a careful consideration of what should constitute the qualifications of those who desire to enter it. The duties of the nurse as a pupil and as an officer in every condition of hospital life follow; and her relation to the public generally is treated exhaustively in the later chapters, the two last taking up the subject of private duty in a clear, comprehensive and satisfactory manner. The book is in fact a treatise on the whole duty of the nurse, and while we cannot follow in detail the handling of the many points brought forward, we can recommend the book as valuable and suggestive, not only to the individual nurse, but to superintendents and teachers in training schools as a medium for systematic instruction. In view of the fact that nursing is pre-eminently one of those occupations in which professional skill should always be supported by personal attributes of a very high and definite order, it might seem surprising that this book is the first of its kind were it not from the fact that it is generally believed that these qualities are inborn and the principles which underlie them cannot be taught through the medium of books. In the training of character, however, which is one of the foremost objects of all modern education, one gladly recognizes as the most helpful agencies much which is out of the beaten track of definite instruction, practical or theoretical, and which helps by guiding and suggesting.

Whatever the author writes about nursing must be accepted as the work of one thoroughly conversant with every aspect of her subject, and as the subject itself is one which occupies a fair share of public attention, the book must have a wide influence.

Diseases of the Tongue. By HENRY T. BUTLIN, F. R. C. S., D. C. L., Surgeon to St. Bartholomew's Hospital, formerly Erasmus Wilson Professor of Pathology and Hunterian Professor of Surgery at the Royal College of Surgeons; and WALTER G. SPENCER, M. S. M. B. (Lond.), F. R. C. S., Surgeon to the Westminster Hospital and in charge of the department of diseases of the nose and throat, formerly Erasmus Wilson Professor of Pathology at the Royal College of Surgeons. Pp. 475, illustrated with eight chromolithographs and thirty-six engravings. (New York: Cassell & Co., Limited, 1900.)

In the twenty-two chapters of this volume are contained in concise form the essential facts with regard to the anatomy of the tongue, all of its usual and unusual diseases and the various methods of treatment, operative and otherwise, which have been undertaken for these affections. The first chapters are devoted to the anatomy of the tongue, congenital defects and inflammatory and other benign affections of the tongue. In discussing the appearances of the tongue under various conditions and the method of their production, Butlin expresses his belief that the results of every-day observations are still extremely indefinite, in spite of the fact that from the earliest times onward attempts have been made to collate the signs exhibited by the tongue with particular diseases as distinguished from constitutional states and to make the tongue serve as an aid in the diagnosis of disease. The tongue is in no way a trustworthy mirror of alterations in the mucous membrane of the intestinal tract. Tuberculosis and syphilis of the tongue and the rarer forms of diseases are thoroughly discussed and will be consulted by all who are specially interested in these subjects. For the general surgeon the chapters dealing with carcinomata will be of greatest interest. Butlin is not disposed to place much importance on predisposing causes of cancer such as syphilis, gout and hereditary tendencies, but exciting causes, particularly irritation by rough and carious teeth, ill-fitting tooth plates and frequent smoking with the rubbing of the stem of the pipe upon the surface of the tongue are thought to have much to do with the causation of carcinoma. Especial stress is laid upon the application of caustics: "If there be one thing more harmful than another in the treatment of simple and indolent sores and affections of the tongue in persons over thirty years of age it is the application of a strong caustic." The diseases most likely to be mistaken for carcinoma in making a diagnosis are syphilitic lumps and sores, tuberculous ulcers, simple warty tumors and simple ulcers and fissures. The resemblance which each one of these diseases at times bears to carcinoma is so great that the difficulty of deciding on the exact nature of the affection is extreme. The therapeutic test is of importance in syphilis, and in cases of doubt it is recommended that a portion of the ulcer should be cut out and examined microscopically. In operating for carcinoma the complete excision with removal of the glands of the neck is favored. The diseased area together with $\frac{3}{4}$ inch of apparently healthy tissue around it in every direction should be removed. As to the importance of removal of the lymphatic glands of the neck, Butlin states that out of 102 patients operated upon, no fewer than twenty-eight had recurrence in the lymphatic glands without recurrence of the disease *in situ*. The mortality for uncomplicated operations is estimated at scarcely 7 per cent, but it rises to more than 20 per cent for excisions below the jaw and to 25 per cent for operations which are complicated by removal of part of the

lower jaw. The number of permanent cures is estimated from a study of statistics at about 20 per cent, but there is thought to be every reason to hope that this percentage, which is still very small, will be greatly improved in the future. At the same time it is probable that carcinoma of the tongue will always remain a very deadly disease. There is appended an extensive bibliography, classified under various headings, covering twenty-four pages.

This book is generally recognized as the most authoritative monograph which has appeared on this subject. It is indispensable for the library of the general surgeon and will prove an important addition, containing many valuable and interesting facts for the library of the general practitioner.

The Thirty-first Annual Report of the State Board of Health. (Boston: Wright & Potter, 1900.)

This report covers the operations of the Board for the year ending Sept. 30, 1899. Dr. H. P. Walcott and Dr. S. W. Abbott continued as president and secretary respectively, positions they have held for many years. There were no changes amongst the other members.

The General Report calls attention to the increased mortality in recent years throughout Massachusetts from local diseases (*i. e.*, of brain, heart, lungs, kidneys, etc.), but this increase is more than counterbalanced by the decrease in deaths from infectious diseases, so that the total death-rate shows a diminution; thus, with an average death-rate for fifty years of 19.5 deaths per 1000 living, the death-rate for 1899 was 17.4.

Smallpox.—There were 105 cases during 1899. From 1883 to 1899 there were 525 cases. Thus one-fifth the total number for these seventeen years occurred in the last year. Since 1885, the fatality (proportion of deaths to cases) was 26 per cent amongst the unvaccinated, 7.6 per cent amongst the vaccinated. Of those attacked by the disease, roughly one-half had been vaccinated; but about half of these had been vaccinated in infancy only. Further interesting details are given p. xvii.

Typhoid fever.—The death-rate continues to show a steady diminution.

Consumption.—The death-rate for the five-year periods from 1851-55 to 1891-95 shows a gradual and fairly steady decrease, from 41.1 per 10,000 living in the former period to 23.1 in the latter. In 1896 the rate was 21.7, dropping steadily to 18.7 in 1899.

Diphtheria.—From 1891 to 1895 the death-rate per 10,000 living fluctuated from 5.3 to 7.4, the fatality varying from 18.9 to 31.7. From 1896 to 1899 the death-rate fell to 2.6 in 1898, rising again to 3.7 in 1899. The fatality steadily diminished from 15.1 in 1896 to 11.5 in 1899.

Isolation hospitals.—This most important factor in the preventive control of infectious diseases is becoming prominent in Massachusetts, one-third of all the cities having provided themselves with hospitals for diphtheria and scarlet fever since 1890. Twice as many cities, however, have provision for smallpox patients, although smallpox is far less common. Not only are these hospitals valuable from a therapeutic standpoint, but the isolation of the patient in them is very much more efficient than it can be at home, and much trouble and expense to the family resulting from the rigid quarantine regulations in force when the patient remains at home are avoided. No question in public health is more pressing than the insuring of the maximum care for infectious patients at the minimum cost in time, trouble and cash to the family. The isolation hospital seems to be the one solution.

Increase of cancer.—The death-rate per 10,000 living in 1856 was males, 1.29; females, 2.45. In 1895, a practically unbroken record of increase ended with death-rates of 4.40 for males, 9.44

for females. While it is probable that greater accuracy in diagnosis accounts for part of this increase, the subject has been considered by the Board worthy of an investigation, which has been entrusted to a commission of physicians who are to report later.

Paris Exposition.—The secretary of the Board, Dr. S. W. Abbott, was invited by the Director of the Department of Social Economy, Education and Hygiene of the United States Commission to prepare a monograph on the progress of hygiene in the United States and to collect an exhibit of subjects pertaining to public health throughout the United States. This exhibition received a "Grand Prix." A gold medal was awarded to Dr. Abbott also in appreciation of his successful work in the matter.

Water supply and sewerage.—The work of the Board in these lines is best shown by a brief review of the main divisions. In 1899, seventy-nine official applications were made to the Board for advice on these subjects, this being the largest number in any year since the Board was established. After the necessary hearings, etc., appropriate action was taken. Chemical and microscopic examinations were made from 212 different sources of water supply, involving some 3500 analyses.

About 90 per cent of the population of this State live in districts having a public water supply. Only two towns with more than 3500 population are unprovided. Of the total population supplied, ten-elevenths receive their water from supplies publicly owned, the remaining one-eleventh from supplies owned by private companies.

By an unfortunate omission, the Acts of 1897, which authorize the State Board to make rules and regulations regarding pollution and to enforce the same, make no provision, in the absence of special legislative appropriations, for the payment of bills so incurred. Thus the action of the Board is unduly hampered.

Summer resorts.—One hundred and thirty or more exist throughout the State. The sanitary conditions of some of these were far from ideal. It has been a matter of remark in Boston for some years that the typhoid fever cases increase in number as soon as the tide of population turns cityward in the autumn, due in part at least to infection during the summer vacation. This factor is an unusually prominent one in Boston because the average wealth is high and with it corresponds the size of the summer exodus.

Under *Water Supply Statistics*, the table on p. 401 showing the water consumption of the various towns and cities, illustrates again the fact that the *per capita* consumption in districts of large population is greater, as a rule, than where the population is small.

Lawrence Experimental Station.—During 1898, many new investigations were begun under H. W. Clark on methods of purifying sewage at high rates of filtration. These were continued during 1899, with additional experiments based upon new points of practical interest developed during their study. The more important of the older intermittent sand filters have been continued in operation. The septic tank has received much attention. Bacterial or contact filters and the use of coarse filtering materials—broken stone, etc.—have been studied.

The treatment in the septic tank of sludge alone was suggested by the observation that the percentage of removal of organic matter increases with the strength of the entering sewage. In September, 1899, the investigation of this subject was begun. The supposed necessity of using a closed tank (to secure the exclusion of light and air) was shown a fallacy, since in the open tank air and light is excluded by the bacteria and fatty scum which form at the surface of the sewage. About two months were required for a septic tank to become fully active, the gas evolved measuring thereafter about 4½ per cent by bulk of the sewage treated. This gas is largely methane and

nitrogen with small quantities of carbon dioxide, carbon monoxide,¹ oxygen and "heavy hydrocarbons." One value of the septic tank treatment, as a preliminary to filtration, lies in the destruction it ensures of the carbonaceous matters (cellulose, paper, etc.) to which the clogging of sewage filters is largely due in the absence of such treatment.

Some interesting work on the removal of *B. coli* from water by sand filters is given. The bacterial efficiency of a filter is generally supposed to be an index of the protection it affords in the removal of typhoid bacilli, should these exist in the applied water. The percentage of removal of *B. coli*—used in this instance as a substitute for the more difficult typhoid bacillus—does not, however, always correspond with the bacterial efficiency; thus, for certain months, the applied water at the city filter was examined both for total bacteria per cc. and for number of *B. coli* per cc. The effluent was also similarly examined. The results ran as follows:

1899.	Total bact. in applied water.	<i>B. coli</i> in applied water.	Total bact. in effluent water.	Bacterial efficiency.	% of times <i>B. coli</i> occurred in effluent. ²	" <i>B. coli</i> efficiency."
Jan.	4900	28	83	98.31	54%	98.08
Feb.	5900	31	108	98.17	62%	98.00
Mar.	6300	19	45	99.30	8%	99.60

The last column of the above table was calculated by the present writer from the data given. The other figures are Mr. Clark's.

It would seem from the above that the efficiency of a filter for *B. coli* lessens more quickly as general bacterial efficiency drops than does this general efficiency itself, but still more striking is the other fact pointed out by Mr. Clark that, within the narrow play of 1.13 per cent variation in an efficiency never below 98.17, the variations in the *frequency* of presence in the effluent of *B. coli* (and by inference in the frequency of presence of typhoid bacilli were they present at all) are very marked.

Mr. Clark also contributes a paper on iron in ground waters. After discussing the various methods for its removal and illustrating each by experiments made on various Massachusetts' supplies, Mr. Clark concludes that different iron-bearing waters may require different methods of treatment for satisfactory purification.

Food and drug inspection.—The annual expense of the food and drug inspection increased from about \$3000 in 1883 to over \$11,000 in 1899. The number of samples examined, however, increased from about 1300 in 1883 to about 9800 in 1899, so that the expenditure per sample, as the report points out, decreased almost one-half.

The milk inspection was devoted mainly to the supervision of dairies, since the local milk inspectors of the various municipalities, while controlling the milk supply after it reaches those municipalities, have no jurisdiction over the sources of origin outside.

The number of prosecutions for adulteration diminished from 150 in 1891 to 47 in 1899 on account of (1st) the reduction of the legal standards of purity or strength; (2nd) the fact that inspectors whose business it is to collect samples gradually become known to the dealers, and it therefore becomes increasingly difficult for them to secure adulterated samples; (3d) the growth of local inspection; (4th) the efforts of the Board to go behind the often innocent retailers to reach the guilty producers, who in many cases reside outside of Massachusetts, which is a manufacturing and not a food-producing State; (5th) the actual improvement in the quality of foods placed on the market.

¹ Prof. L. P. Kinnicutt states as the result of recent investigations that the gas recorded as carbon monoxide gives certain carbon monoxide reactions, but is not carbon monoxide. Its identity has not yet been determined.

² Each time *B. coli* was found, not more than one colony per cc. was probably present.

The report of the analyst, Albert E. Leach, is particularly valuable this year, since it gives the methods of analysis used. There are comparatively few food and drug experts in this country, but the ways in which adulterations are detected should be of interest to all consumers as well as to those scientifically inclined. It is true that the publication of the methods of analysis may afford to keen-witted, would-be adulterators suggestions for new ways of "beating the game," but it is the business of the expert to so conduct his investigations that he cannot be deceived. However keen the adulterators may be, the expert has the greater weight of scientific knowledge and experience behind him. Moreover, "thrice is he armed who hath his quarrel just."

Experiments on the solvent action of fruit acids on tin, bearing upon possible poisoning from canned goods, showed that most of the solution occurs in the first three months. The percentages of tin taken up by different strengths of different acids were determined.

An ingenious device for the deception of the public is that practiced by a certain baking powder concern, which advertises "All grocers are authorized to guarantee bread, etc.," made with this powder free from alum, ammonia, etc. It is to be noted that no claim is made that the powder is free from these substances; indeed, as a matter of fact, it contains both alum and ammonia, but the advertisement is true to the extent that in the preparation of bread, etc., the alum is converted into aluminum hydrate and the ammonia is driven off!

In the collecting of samples of drugs, lists of the articles wanted were furnished to various druggists. In some cases they interpreted these lists as prescriptions, so that the analyst received rather startling mixtures of such incompatibles as hydrobromic acid, silver nitrate and bicarbonate of soda!

Pathological and Bacteriological Laboratory.—Since 1895, Dr. Theobald Smith has manufactured from 65 million to 75 million units of diphtheria antitoxin. The strength of this antitoxin has varied from 200 to 400 units per cc. The amounts used per case are shown in a table on p. 657, reaching over 100,000 units for one patient in one instance. The total fatality of cases treated for five years is 11.2 per cent.

A summary of the diagnostic work of the Board follows and the volume ends with *Statistical Summaries* and condensed reports from the different cities and towns of the State.

Amongst the latter are some interesting accounts of *typhoid epidemics* traced to their sources, so far as was possible, by Dr. F. L. Morse, Medical Inspector of the Board. (See pages 737, 744, 754, etc.) In one of the epidemics described (p. 761) the infection was very clearly shown to be carried by celery which had been manured with undisinfected typhoid feces.

The impossibility of reaching an absolute decision as to the source of infection in the majority of typhoid epidemics is well illustrated by some of these accounts and should impress every one with the importance of reporting every epidemic in which the source may be indubitable, that the bulwarks of our faith in these matters may be duly strengthened from time to time. Too often it happens that the expert is called in so long after the source of infection has disappeared that only very tangled threads of evidence remain and the Scotch verdict of "not proven" must frequently be the sum total attained by prolonged and conscientious work. It is better to render such a verdict than one, which, while more definite in terms, is based upon evidence not wholly conclusive.

It is difficult to discriminate between the successive yearly reports of the Board, since all have been so excellent, but it is true that from a technical standpoint the present report will be of more interest to laboratory men than are those of the two or three preceding years. Particularly is this true of the reports, already briefly outlined, from Mr. Clark and Mr.

Leach. The material of the latter's report recalls somewhat those earlier days when methods of analysis received treatment so instructive that the publications of the Board really formed technical text-books of a high order.

We must again regret the absence of other than a merely formal contribution from Dr. Theobald Smith. Indeed all the few faults of this report are those of omission, not of commission. Needless to say the typography is, as usual, above reproach.

HIBBERT WINSLOW HILL.

Practice of Medicine. A Text-book for Practitioners and Students, with Special Reference to Diagnosis and Treatment. By JAMES TYSON, M. D., Professor of Medicine in the University of Pennsylvania, and Physician to the Hospital of the University. Second edition, thoroughly revised and in parts rewritten. With 127 illustrations. (Philadelphia: P. Blakiston's Son & Co., 1900.)

The first edition of this admirable text-book appeared in 1896. It was most favorably reviewed in this journal in June, 1897. The second edition has been thoroughly revised and in part rewritten. This has been done with only a moderate increase in the number of pages of printed matter, the present edition containing 1222 pages. The revision has been largely made in the sections on infectious and nervous diseases. The section on Diseases of the Nervous System has been revised by Dr. William G. Spiller, which is sufficient guarantee for its having been thoroughly done and for the subject being brought up to date. We should like to have seen the subject of Neurasthenia dealt with more fully, however. Only three pages are devoted to it, which seems entirely insufficient considering the prevalence of the affection. There is probably no affection that the general practitioner appreciates or understands less, nor is there one, the treatment of which, gives him more annoyance and worry.

We occasionally observe that a recent clinical finding of importance in the symptomatology or diagnosis of a disease has escaped the notice of the author. For instance, we may call attention to the fact that no mention is made of the marked eosinophilia which is present in the acute stages of nearly all cases of trichinosis. This is one of the most valuable observations on the blood in any disease in recent years, and has been the feature that has attracted the attention of the observer to the possibility of an infection with trichinae in so many of the recently reported cases.

In nearly every respect, however, the book is an admirable one. We know of no text-book on the practice of medicine that is more profusely illustrated by charts and plates. We predict for it the same success that attended the publication of the first edition.

Introduction to the Study of Medicine. By G. H. ROGER, Professor Extraordinary in the Faculty of Medicine of Paris. Authorized translation by M. S. GABRIEL, M. D. With additions by the author. (New York: D. Appleton & Co., 1901.)

This is in every way a most admirable book. It is based on a course of lectures delivered by Dr. Roger at the University of Paris during the session of 1897-98. The translator has done students and practitioners in this country a great service by the publication of this edition in English. The volume has been brought up to date by additions and corrections made by the author.

The work, which contains 545 pages, is in no sense intended to take the place of a text-book on the practice of medicine. The various diseases are not treated in detail, but the object has been to give the student who is just entering the practical stage of the study of medicine a thorough and broad understanding of the general principles which underlie disease. The object of the author will be appreciated best by quoting the following lines

from his preface: "We all know from experience how much time is wasted by not knowing with what subject to begin, what books to read, and also by being compelled frequently to refer to a dictionary for an explanation of technical terms encountered. With the view of relieving beginners of much useless embarrassment, the Faculty of Medicine intrusted me with the course of lectures which I now publish."

The first seven chapters are devoted to a description of how an individual becomes sick. The causes are considered under the heading of mechanical, physical and animate agents. Under the latter he takes up the general bacteriology of disease. He then proceeds to show how infection of the human organism takes place.

The sections devoted to disturbances of nutrition, heredity and inflammation are of unusual interest. We know of no text-book in which the important problems connected with heredity are presented so thoroughly and in so interesting a manner.

The author emphasizes the importance of careful observation of the case under treatment, and the proper interpretation of the conditions and physical signs found. The chapters on semiology are of great value to the student in teaching him the proper method of observing and examining a patient. The book concludes with chapters dealing with the general considerations which should guide one in making a diagnosis or prognosis of a case and in outlining its treatment.

This book will be found of great service not only to the beginner, but also to the advanced student in medicine, as well as to practitioners. We know of no book of its kind in English. It is filled with practical points which are not found in the ordinary text-books of medicine. The book makes interesting reading and the translator has apparently done justice to the original edition.

Medical and Surgical Reports of the Boston City Hospital. Eleventh Series. Edited by HERRBERT L. BURRELL, M. D.; W. T. COUNCILMAN, M. D., and CHARLES F. WITHINGTON, M. D. (Boston: Published by the Trustees, 1900.)

The volume of the Reports of the Boston City Hospital for 1900 contains twenty separate papers on medical and surgical subjects, with a total of 254 pages. A special appropriation has enabled the editors to illustrate the reports this year. There are several papers of especial interest, only a few of which can be referred to in this review.

Lund reports six cases of acute hæmorrhagic pancreatitis from the standpoint of the surgical treatment. Five of the cases were in women, and four of these also had gall-stones. In no case was a definite diagnosis made. Five of the cases were operated on, with one recovery.

Jackson gives an analysis of 59 cases of malignant endocarditis. In 43 cases the diagnosis was confirmed at autopsy. Cultures were made in 23 cases, organisms being obtained in pure culture in 19. The *Streptococcus pyogenes* was obtained in 8 cases, pneumococcus in 5, *Staphylococcus aureus* in 3, *Colon bacillus* in 1, *Staphylococci* and *Streptococci* in 1, *Streptococcus* and others in 1. The distribution of the lesion in the 43 cases was as follows: Aortic valves, 9 cases; aortic and mitral valves, 10 cases; mitral valve, 15 cases; right side of the heart, 6 cases; endocardium of ventricle, 3 cases.

Bottomley reports 28 cases of tuberculous peritonitis in which operative treatment had been adopted. Cases were considered recovered only when they returned well at least one year after

the operation. Of the series, 11 recovered; the same number died. Two cases improved and 4 cases could not be traced.

Low gives the bacteriological findings in 100 cases of acute appendicitis. The results were as follows: *Streptococcus pyogenes* (pure culture), 2; *Streptococcus pyogenes* or *diplococcus lanceolatus* and *Bacillus coli communis*, 61; *Streptococcus pyogenes* and intestinal saprophytes, 15; *Bacillus coli communis* (pure culture), 8; *Bacillus coli communis* and unidentified cocci, 13; *Bacillus lactis aerogenes* and *Bacillus pyocyaneus*, 1.

Thomas and Hibbard have an interesting paper on Heart Failure in Diphtheria. They think that one death in five from diphtheria is due to heart failure. The complication is more frequent in children than in adults, and occurs most frequently in the second week of the disease.

Diseases of the Heart: Their Diagnosis and Treatment. By ALBERT ABRAMS, A. M., M. D., (Heidelberg), F. R. M. S. (Chicago: G. P. Engelhard & Co., 1900.)

This little volume of 170 pages contains a fund of information on cardiac diseases with a concise review of their symptomatology, physical signs and treatment. The subject is rather attractively presented. The author states that the book was never intended to aspire to the dignity of a treatise on diseases of the heart, but that the primary object was to make it useful to the practical physician in the diagnosis of cardiac diseases. The personal experience of the author is frequently met with throughout the volume. Whereas we can hardly see the need for such a compendium as this book is, it will no doubt be found of material aid to the general practitioner who has not the time to consult a more extensive treatise on the subject.

BOOKS RECEIVED.

Essentials of the Diseases of Children. Arranged in the Form of Questions and Answers. Prepared Especially for Students of Medicine. By William M. Powell, M. D. Third edition, thoroughly revised by Alfred Hand, Jr., A. B., M. D. (Saunders' Question-Compends, No. 15.) 1901. 12mo. 259 pages. W. B. Saunders & Company, Philadelphia and London.

Atlas and Epitome of Labor and Operative Obstetrics. By Dr. Oskar Schaeffer. Authorized translation from the fifth revised German edition. Edited by J. Clifton Edgar, A. M., M. D. With 14 Lithographic Plates in Colors and in 139 other Illustrations. (Saunders' Medical Hand-Atlases.) 1901. 12mo. 111 pages. W. B. Saunders & Company, Philadelphia and London.

Principles of Surgery. By N. Senn, M. D., Ph. D., LL. D. Third edition, thoroughly revised. With 230 Wood-engravings, Half-tones, and Colored Illustrations. 1901. 8vo. xv + 699 pages. F. A. Davis Company, Philadelphia and Chicago.

Atlas and Epitome of Ophthalmoscopy and Ophthalmoscopic Diagnosis. By Prof. Dr. O. Haab, of Zurich. Authorized translation from the third revised and enlarged German edition. Edited by G. E. de Schweinitz, A. M., M. D. With 152 Colored Lithographic Illustrations. (Saunders' Medical Hand-Atlases.) 1901. 12mo. 85 pages. W. B. Saunders & Company, Philadelphia and London.

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GENERAL STATEMENT.

The Medical Department of the Johns Hopkins University was opened for the instruction of students October, 1893. This School of Medicine is an integral and coördinate part of the Johns Hopkins University, and it also derives great advantages from its close affiliation with the Johns Hopkins Hospital. The required period of study for the degree of Doctor of Medicine is four years. The academic year begins on the first of October and ends the middle of June, with short recesses at Christmas and Easter. Men and women are admitted upon the same terms.

In the methods of instruction especial emphasis is laid upon practical work in the Laboratories and in the Dispensary and Wards of the Hospital. While the aim of the School is primarily to train practitioners of medicine and surgery, it is recognized that the medical art should rest upon a suitable preliminary education and upon thorough training in the medical sciences. The first two years of the course are devoted mainly to practical work, combined with demonstrations, recitations and, when deemed necessary, lectures, in the Laboratories of Anatomy, Physiology, Physiological Chemistry, Pharmacology and Toxicology, Pathology and Bacteriology. During the last two years the student is given abundant opportunity for the personal study of cases of disease, his time being spent largely in the Hospital Wards and Dispensary and in the Clinical Laboratories. Especially advantageous for thorough clinical training are the arrangements by which the students, divided into groups, engage in practical work in the Dispensary, and throughout the fourth year serve as clinical clerks and surgical dressers in the wards of the Hospital.

REQUIREMENTS FOR ADMISSION.

As candidates for the degree of Doctor of Medicine the school receives:

1. Those who have satisfactorily completed the Chemical-Biological course which leads to the A. B. degree in this university.
2. Graduates of approved colleges or scientific schools who can furnish evidence: (a) That they have acquaintance with Latin and a good reading knowledge of French and German; (b) That they have such knowledge of physics, chemistry, and biology as is imparted by the regular minor courses given in these subjects in this university.

The phrase "a minor course," as here employed, means a course that requires a year for its completion. In physics, four class-room exercises and three hours a week in the laboratory are required; in chemistry and biology, four class-room exercises and five hours a week in the laboratory in each subject.

3. Those who give evidence by examination that they possess the general education implied by a degree in arts or in science from an approved college or scientific school, and the knowledge of French, German, Latin, physics, chemistry, and biology above indicated.

Applicants for admission will receive blanks to be filled out relating to their previous courses of study.

They are required to furnish certificates from officers of the college or scientific schools where they have studied, as to the courses pursued in physics, chemistry and biology. If such certificates are satisfactory, no examination in these subjects will be required from those who possess a degree in arts or science from an approved college or scientific school.

Candidates who have not received a degree in arts or in science from an approved college or scientific school will be required (1) to pass, at the beginning of the session in October, the matriculation examination for admission to the collegiate department of the Johns Hopkins University, (2) then to pass examinations equivalent to those taken by students completing the Chemical-Biological course which leads to the A. B. degree in this University, and (3) to furnish satisfactory certificates that they have had the requisite laboratory training as specified above. It is expected that only in very rare instances will applicants who do not possess a degree in arts or science be able to meet these requirements for admission.

Hearers and special workers, not candidates for a degree, will be received at the discretion of the Faculty.

ADMISSION TO ADVANCED STANDING.

Applicants for admission to advanced standing must furnish evidence (1) that the foregoing terms of admission as regards preliminary training have been fulfilled, (2) that courses equivalent in kind and amount to those given here, preceding that year of the course for admission to which application is made, have been satisfactorily completed, and (3) must pass examinations at the beginning of the session in October in all the subjects that have been already pursued by the class to which admission is sought. Certificates of standing elsewhere cannot be accepted in place of these examinations.

SPECIAL COURSES FOR GRADUATES IN MEDICINE.

Since the opening of the Johns Hopkins Hospital in 1889, courses of instruction have been offered to graduates in medicine. The attendance upon these courses has steadily increased with each succeeding year and indicates gratifying appreciation of the special advantages here afforded. With the completed organization of the Medical School, it was found necessary to give the courses intended especially for physicians at a later period of the academic year than that hitherto selected. It is, however, believed that the period now chosen for this purpose is more convenient for the majority of those desiring to take the courses than the former one. The special courses of instruction for graduates in medicine are now given annually during the months of May and June. During April there is a preliminary course in Normal Histology. These courses are in Pathology, Bacteriology, Clinical Microscopy, General Medicine, Surgery, Gynecology, Dermatology, Diseases of Children, Diseases of the Nervous System, Genito-Urinary Diseases, Laryngology and Rhinology, and Ophthalmology and Otology. The instruction is intended to meet the requirements of practitioners of medicine, and is almost wholly of a practical character. It includes laboratory courses, demonstrations, bedside teaching, and clinical instruction in the wards, dispensary, amphitheatre, and operating-rooms of the Hospital. These courses are open to those who have taken a medical degree and who give evidence satisfactory to the several instructors that they are prepared to profit by the opportunities here offered. The number of students who can be accommodated in some of the practical courses is necessarily limited. For these the places are assigned according to the date of application.

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THE MEDICINE AND DOCTORS OF HORACE.

BY EUGENE F. CORDELL, M. D.

(Read before the Johns Hopkins Hospital Historical Club, November 12, 1900.)

In all ages of the world the doctor and his practice have been the shuttlecock of the wits and satirists. That medicine has not perished under these assaults must be ascribed to the unlimited faith of the human mind and to the heaven of good that even in the darkest period of its history has been mingled with its shortcomings and errors. In selecting an author of the Augustan age as representative of its sentiment and inspiration, none occurs to us with more convincing readiness than the great wit and lyric poet, the satirist of Roman manners and morals, the boon companion of Augustus and his prime minister, whose name heads this page. What has Horace to say of the doctors and medicine of his day?

It is a singular fact that nowhere in all his extant writings is there a word of unkindness or ridicule of the professors of medicine. Of few writers of his stamp could such

a statement be made. His allusions are always kindly and breathe unfeigned respect and confidence. This will surprise us the more, when we reflect upon the character of the Roman profession of his day, just emerging from obscurity and chiefly in the hands of slaves and foreign adventurers, bent in most cases solely upon self-aggrandizement. Writing to a friend,¹ he gives this advice: "If your side or kidney should be attacked with an acute disease, seek a remedy for the disease," or as Sir Theodore Martin puts it:²

"If spasms of pain assail your sides or back,
Send for the doctor; set him on the track
The mischief's cause and cure upon the spot."

¹ Epist. I, 6, 28.

² Metrical translation.

In another place he says:³ "If no quantity of water would put an end to your thirst, you would tell it to your physicians."

And again:⁴ "The false modesty of fools will conceal ulcers rather than have them cured."

During the latter half of the poet's life his health was poor, the first evidence of failure manifesting itself on the journey to Brundisium, when he was 28, in an inflammation of the eyes: "Here, having got sore eyes, I was compelled to smear black ointment on them."⁵ He was also, like Virgil, a martyr to weak digestion. It is probable also that he had some affection of the chest, as in addressing his mistress Lyce, he says:⁶ "This side of mine will not always be able to endure your threshold and the rain," and in Epist. I, 7, 26, he speaks of his "*non forte latus*."

He must, therefore, have been brought into frequent contact with physicians in a professional way and it must be considered indeed remarkable that no word of blame or reproach of them escapes him. Take the case of the court physician, Antonius Musa. Horace was in the habit of spending his winters at Baiae, a beautiful seaside resort in Campania, not far from Naples. Here were hot medicinal waters, pleasant and wholesome, and a mild air. The wealthy Romans built their villas around and the brilliant society of Rome was transported thither during the cold weather. Horace never tires of singing the delights of "watery Baiae."

"Baiae's waters fair
With happy heart I hail."⁷
"No bay in all the world so sweet, so fair,
As may with Baiae, Dives cries, compare."⁸
"Should winter swathe the Alban fields in snow,
Down to the sea your poet means to go,
To nurse his ailments and in cosy nooks,
Close huddled up, to loiter o'er his books."⁹

Now imagine this small, frail, prematurely gray poet, with his weak digestion, his sore eyes, his "*non forte latus*," and his nervous temperament, "one to whom warmth is life,"¹⁰ ordered by the medical autocrat of Rome, to give up his dear Baiae and go to take the cold baths at Velia or Salernum and this in midwinter. Ugh! he shivers at the thought, and yet no word of reproach escapes him—he has no thought of disobeying.

Horace also seems to reprobate ignorant handling of drugs in the following quotation:

"Where is the man * * *
Who ventures to administer a draught,
Without due training in the doctor's craft?
Doctors prescribe who understand the rules,
And only workmen handle workmen's tools,"¹¹

or to use a literal translation (and more fully):

"He that is ignorant of a ship is afraid to work a ship; none but he who has learned dares administer (even) south-

ernwood to the sick; physicians undertake what belong to physicians; mechanics handle tools, but we learned and unlearned, promiscuously write poems."

Horace, evidently speaking from his personal experience, inculcates a sparing and plain diet. To his friend, Iccius, he says:¹²

"Si ventri bene, si lateri est, pedibusque tuis, nil
Divitiæ poterunt regales addere majus,"

or, as Theodore Martin translates it:

"Let your digestion be but sound,
Your side unwrung by spasm or stich,
Your foot unconscious of a twitch,
And could you be more truly blest,
Though of the wealth of kings possessed?"

This definition of health corresponds nearly with the soundness of "limb, wind and pizzle," which traders in horses are used to demand.

The word *medicus* occurs nine times in the writings of Horace. Addressing an imaginary miser, in Satire I, 1, 80, he says: "If your body should become disordered by being seized with a cold, or any other casualty should confine you to your bed, is there any one upon whom you can rely to stay with you, prepare the fomentations and beseech the doctor to bring you back to health and restore you to your children and dear relatives?" This passage recalls a letter written by Cicero to his learned freedman, Tiro, in which he urges the invalid to spare no expense—"another fee to the doctor may make him more attentive."¹³

Opimius, another miser, who thinks himself poor, although surrounded by heaps of silver and gold, is seized with a prodigious lethargy.¹⁴ His heir, with unconcealed joy, is scouring about the house in search of keys and coffers. Then the quick-witted and faithful physician rouses his patient in the following way: He orders a table to be brought in and the bags of money to be poured out upon it and several persons to begin counting it. At the ring of the coin, the sick man jumps upon his feet, whereupon the doctor addresses him thus: "Do you not know that your ravenous heir will carry off your treasures unless you watch them?" "Not while I am still alive?" "Why, certainly; rouse yourself, man!" "But what must I do?" "Why, you must have food and restoratives; you are almost bloodless, already. Come no foolishness, take this bowl of gruel." "How much did it cost?" "Oh, a trifle." "But tell me exactly." "Two pence." "Alas! what does it matter whether I die of disease or by robbery and extravagance?" The disinterested character of the doctor is well brought out in this scene.

"O Jupiter!"¹⁵ thou who causest men to suffer and removest their afflictions (cries the mother of a boy confined

¹² Epist. I, 12, 5.

¹³ "Roman Life in the Days of Cicero," by Prof. Church, 1881.

¹⁴ Sat. II, 3, 142. See Celsus Lib. III, 20, who says it is a dangerous acute disease with paroxysms and fever, probably congestive chill.

¹⁵ Sat. II, 3, 88.

³ Epist. II, 2, 46. ⁴ Epist. I, 16, 24. ⁵ Sat. I, 5, 30. ⁶ Od. III, 10, 19.

⁷ Martin, Od. III, 4, 24. ⁸ Martin, Epist. I, 1, 83. ⁹ Martin, Epist. I, 7, 10. ¹⁰ Epist. I, 20, 24. ¹¹ Martin, Epist. II, 1, 114.

to bed for five months), if this quartan chill shall at thy command leave my child, on thy fast day he shall be placed naked in the Tiber.' Should chance or the doctor relieve the patient from his imminent danger, the superstitious mother will destroy her child by placing him on the cold bank and bringing back the fever."

"A new disorder expelled the old in a miraculous manner, as it is accustomed to do, when the pain of the afflicted side or head is turned upon the stomach; or as it is with a man in a lethargy, when he turns boxer and attacks his physician."^{15a}

To Maecenas, he writes:¹⁶ "In this case" (*i. e.*, where the judgment is disordered), "you think me mad, only as the generality of men are mad, and you do not laugh or believe that I stand in need of a doctor, or of a guardian assigned by the praetor."

To his friend Celsus, he writes,¹⁷ more of his mental than his physical troubles, "Diseased as I am, I am willing to hear nothing which may relieve me, I am displeased with my faithful physicians and am angry with my friends for their unceasing efforts to rouse me from my fatal lethargy."

To Augustus, he writes:¹⁸ "He that knows naught of ships will be afraid to work one; none but those who have been taught will dare administer to the sick even a dose of southernwood; mechanics handle tools, doctors stick to their medicines, whilst we poets write verses whether we are learned or unlearned."

To his friend, Julius Florus,¹⁹ he writes: "If no abundance of water should relieve your thirst, you would tell it to your physicians."

Horace mentions by name two physicians—Antonius Musa and Craterus; perhaps a third person of distinguished medical attainments is named—I will discuss this question later.

Antonius Musa, a highly educated Greek freedman of Augustus, was led to the study of medicine by a desire to relieve his father, who suffered from great infirmities. He acquired very great honor and distinction by curing his master of a severe attack of illness, which had resisted all previous attempts at cure, and seemed likely to prove fatal. Of the nature of this attack we are not positively informed (some say gout) but it had been treated by hot fomentations and sweating without relief. The case seeming so desperate, a change of physicians was determined upon and Musa was placed in charge. Bold and decisive action seemed to be demanded and consequently the entire previous method of treatment was reversed. Cold douches were freely applied and the august patient was drenched with draughts of cold water. With these measures, whether *post* or *propter hoc*, he recovered and, although his health was always delicate, he lived for 36 years after this critical illness. By this happy termination, the physician reaped a rich reward. He was invested with citizenship and the order of knighthood; a large sum of money was bestowed

upon him by Augustus and the Senate, and his statue in brass, erected by public subscription, was placed by the side of that of the God of Medicine, in the temple of Aesculapius, which stood on an island in the Tiber. Nor did he alone profit by his good fortune; it was shared in large measure by all the disciples of Hippocrates in Rome, who now, for the first time, acquired citizenship, and were relieved from all civil burdens. The Methodists—the sect to which Musa belonged—naturally profited most by this elevation and became the predominant body in the profession of the Roman capital. Cold bathing became of course the fashionable fad, and winter offered no bar to its use. In Epist. I, 15, Horace asks his friend Caius Neumnus Vala about Velia and Salernum, two winter resorts; he wants to know about their climate and air, their people, roads, water, corn, fish, hares and boars. He had long been in the habit of spending his winters at Baiæ, where there were warm sulphur springs famous in the treatment of nervous disorders. But now that delightful resort is deserted, its myrtle groves are silent and the villagers are murmuring against the fashionable physician, who has deprived them of their patronage and Horace is preparing to follow Musa's directions and the crowd, and seek waters less relaxing and of lower temperature. Musa was also the physician of Maecenas, and it is related that he employed the distant murmuring of falling water for that statesman's terrible insomnia, obtaining, however, only temporary relief by this measure for his patient, everything failing at last. He was the intimate friend of Virgil, who praises his taste and skill in an epigram, affirming that he was loaded with all the favors of Apollo and the muses.²⁰ He is spoken of by Dion Cassius, Caius Plinius Secundus and Galen. The last-named quotes him frequently. Strange to say he is not mentioned by Celsus. He introduced into practice the lettuce, chicory and endive and was the author of several pharmaceutical works of which only a few fragments remain. These were collected and published by Flor. Caldani, in 8vo, Bassano, 1800. Several medicinal compositions bearing his name enjoyed celebrity for a long time. Musa had a brother, Euphorbus, who was physician to Juba, King of Mauritania, and who discovered and gave his name to the plant Euphorbia.

In the imaginary conversation in which Damasippus maintains that most men are mad,²¹ the philosopher Stertinus is represented as saying: "Suppose that Craterus" [the physician] "should pronounce a patient free from disease of the stomach" [*non cardiacus*],²² "is he therefore well and shall he get up? No, the doctor will forbid that because he is suffering from an acute pleurisy or nephritis." And so he argues, if a man is not insane in one direction, he is in another. Craterus was likewise a Greek, and stood in high

^{15a} Sat. II, 3, 27.

¹⁶ Epist. I, 1, 101.

¹⁷ Epist. I, 8, 7.

¹⁸ Epist. II, 1, 114.

¹⁹ Epist. II, 2, 146.

²⁰ Virgil's Catalecta. ²¹ Sat. II, 3.

²² Hecker believes that the disease known as "*Cardiacus*" has disappeared and that it was peculiar to antiquity. Védrenès, *Traité de Celse*, Paris, 1876.

repute in Rome; Sir Theodore Martin calls him the "Abernethy of his day." He is mentioned a number of times by Galen. Cicero writes to his friend Pomponius Atticus (B. C. 45) upon hearing of the illness of the latter's daughter: "*De Attica doleo*"—"credo autem Cratero." Persius writes:²³

"Venienti occurrere morbo,
Et quid opus Cratero magnos promittere montes,"

"meet the disease at its first stage and what occasion is there to promise Craterus gold mines for a cure?" Porphyry²⁴ gives an account of the cure by him of a slave attacked with a horrible disease, in which the flesh separated from the bones. He also invented an antidote against the sting or bite of venomous animals.

The name Celsus occurs twice in the writings of Horace—Epist. I, 3 and Epist. I, 8. The first is addressed to Julius Florus, who has gone to Asia Minor, 20 B. C., A. U. C. 733, as companion of Claudius Tiberius Nero, Augustus' stepson and successor in the imperial chair. Tiberius, who was himself but 22, was accompanied on this occasion (his Armenian expedition), by a number of young Romans of taste and genius—the "*studiosa cohors*," as Horace calls them—among whom were philosophers, historians, orators, poets and doubtless a physician or two. "What works is the studious train pursuing?" asks the poet. Among others he refers to one named Celsus, and in the following words: "What is my dear Celsus about? already advised he shall be advised again and again,"²⁵ to collect treasures of his own, and to let alone writings, which are stored in [the library of] the Palatine Apollo, lest, if it should chance that the flock of birds should hereafter come to claim their feathers, he, like the jackdaw, should be stripped of his stolen colors and become the subject of ridicule." The reference is to the well-known fable of Aesop. The library here referred to was one which had been founded by the Emperor Augustus in his palace on the Palatine Hill, next to the temple of the god. It was designed for the use and encouragement of literary men and is several times referred to by Horace.²⁶ Here was collected the literature of the world, all the writings which were judged worthy of "cedar and immortality." Hither gathered scholars of every kind to consult the literary treasures, and it is said that the physicians here gave instruction to their pupils. The question naturally arises—may not the great medical writer Celsus have here prepared those compilations of philosophy and medicine, of which the eight books "*De Medicina*," written in most elegant Latin alone survive to this day? May not the young Celsus mentioned by Horace have been the great author himself?

Epist. I, 8 was addressed to *Celsus Albinovanus*, whom Horace describes as the attendant and secretary of Tiberius Claudius Nero, the general in the Armenian campaign al-

ready referred to. The use of medical terms in this epistle is somewhat significant: "I will hear nothing, learn nothing that may alleviate my sickness; I am displeased with my faithful physicians, I am angry with my friends who are striving earnestly to rouse me from my fatal lethargy." The whole tenor of these letters shows that the greatest intimacy must have existed between the writer and young Celsus, and that the former entertained for the latter an interest which was both fatherly and disinterested, for the language, as has been remarked by Orelli and others, was not intended in any offensive sense.

Now we know almost nothing about the medical writer Celsus. The date and place of his birth, residence and death, are alike unknown. Even his name is in doubt, some maintaining that the first initial "A," stood for Aulus, others that it meant Aurelius. That he was a member of the Cornelian family, to which so many illustrious men belonged, indicates a patrician rank. It is uncertain whether he was a practicing physician, with the probabilities much in favor of the negative; yet his minute and accurate descriptions of diseases, instruments and operations, his profound and independent judgment and his frequent references to his personal experience, show a practical knowledge of the subject which could only have come from prolonged observation and actual participation.

What we do know of him is that he compiled a great encyclopædic work on various branches of learning of which his eight books on medicine alone survive to this day. The extent of this work, and the versatility of its author, are shown by its embracing elaborate treatises on rhetoric, philosophy, military science, agriculture (including a section on veterinary science) and medicine. According to Gurlt,²⁷ this compilation occupied some fifty or more years of the author's life, the part on rhetoric having been written in the last decennium before Christ and that on medicine at the beginning of the fifth decennium after Christ under the Emperor Claudius. The treatise on medicine was the first medical work written in the Latin language and the most important one of antiquity after Hippocrates. To it we owe almost all that we know of the previous 400 years, and of the great Alexandrian School of anatomists and surgeons. Our high estimate of it is not invalidated by the fact that it was written for laymen, or by the neglect which it met at the hands of Celsus' contemporaries and successors for many centuries, in fact until the revival of learning in the 15th century. Its purity of style and literary excellence render it a worthy companion of the great non-medical classics of the Augustan age and have caused Celsus to be termed the "*Cicero Medicorum*." That it was not appreciated by the profession of Rome is probably to be attributed to two circumstances: 1, That it was addressed to laymen; 2, that the profession of Rome was made up almost entirely of Greek physicians.

²³ Sat. III, 64. ²⁴ *De Abstinencia ab Animalibus*, I, 17, 61.

²⁵ Of the use of the verb *moneo* here I find this in Gulielmus Braunhardus, "*Quinti Horatii Flacci, Opera Omnia*," Leipzig, 1835: "*monemus jure quodam nostro et auctoritate; hortamur fere argumentis, Cruq.*"

²⁶ Sat. I, 4, 22; Sat. II, 10, 38; Epist. II, 1, 216; Epist. II, 2, 94.

²⁷ *Geschichte der Chirurgie*, Vol. 1. See also Bähr, *Geschichte der Röm. Literatur*.

Is it possible to identify the Celsus of Horace with the Celsus of medicine? It would have been nothing unusual, if the young courtier, who had been honored by Tiberius with the appointment of secretary, were well acquainted with medical science, for it constituted, no less than philosophy, a part of the education of all high-born Romans, who often found in the "ampla valetudinaria,"²⁸ upon their large country estates, abundant opportunities for the practical exercise of such knowledge. Again, to write such a work as that of A. Cornelius Celsus, required access to a very large collection of books, such as he would have found nowhere in Italy except in Rome. He must therefore have repaired to Rome, if not already a resident of the metropolis, in order to carry on his researches, and if this be granted, where would he have found such opportunities for work as in the great collection of Augustus—the public library on the Palatine Hill? Here then, we find two men of the name of Celsus, simultaneously engaged in transcribing and compiling, not once but habitually and evidently for publication. What is the inevitable inference? That they are one and the same person.

The name, *Albinovanus*, seems at first sight to offer an insurmountable obstacle to this theory. Let us consider, briefly, the nomenclature of Roman proper names. Every free-born Roman of the higher class had three names, I. an individual name or prænomen, as Aulus, Caius, Marcus, Publius, Quintus, etc. The number of these was limited. They were considered titles of honor and as such were highly prized, as Horace says: "*gaudent prænominibus molles auriculæ.*"²⁹ II. The gens name or nomen, as Claudius, Cornelius, Julius, Tullius, Virgilius. III. The individual family name or cognomen, as Crispus, Maro, Naso, Plautus, Seneca. The cognomen was sometimes assumed, "*optivum cognomen*"; often it was conferred by the public:

"frequentia Mercuriale
Imposuere mihi cognomen compita,"³¹

"the crowded streets gave me the surname Mercurial." I imagine that such cognomina as *canis*,³² *pinguis*,³³ *Asina*^{33a} and *Asellus*,^{33b} were rather in the nature of nicknames; they would hardly have been adopted voluntarily by their holders. An additional cognomen was often added to a name to indicate some circumstance of life, or character. In later times this was called "*agnomen*." Such were *Africanus*, *Asiaticus*, *Numantinus*, *Capitolinus*, *Torquatus*, *Germanicus*, *Justus*, *Felix*, *Declamator*. Thus are *Publius Cornelius Scipio Africanus*, *Lucius Cornelius Scipio Asiaticus*, *Publius Aemilianus Scipio Numantinus*, *Lucius Annæus Seneca Declamator*, *Lucius Calpurnius Piso Frugi*, *Decius Junius Brutus Scaeva* and *Albinus*, *Quintus Fabius Maximus Cunctator*, *Spurius Postumius Albinus Magnus* and *Regillensis*, and many others. Sometimes in the case of very distinguished men there was more than one of these additional cognomina or titles, and it was no unusual thing for names to undergo

change in course of time, old titles being dropped and new ones assumed. Among friends, the mode of address was usually by the gens nomen or the cognomen, the prænomen being reserved for formal or polite address, something like Mr., Rev., Dr., Sir. In eight of the epistles of Horace, omitting doubtful ones, his correspondents are addressed by their cognomina; in six the gens name is used and in one both; not once is the prænomen used. The same rule prevails throughout the entire work, the prænomen never being employed. The poet refers to himself most often as *Horatius*, once only as *Flaccus* and once as *Quintus*. Of Latin authors who mention him, according to Horace Delphini, eight speak of him as *Horatius* and five as *Flaccus*. From all this, we may conclude that in "*Celsus Albinovanus*" the poet has omitted part of the name of his friend, quite certainly the prænomen and most probably the gens name also, especially as we never find "*Celsus*" used in this sense. "*Celsus*," then being the cognomen or third name, what shall we say of "*Albinovanus*." Its position here, as well as in the names *Marcus Tullius Albinovanus*, *Caius Pedo Albinovanus* and *Publius Tullius Albinovanus* also mentioned in the literature, show that it was a cognomen and not a family or gens name, one therefore least important and most liable to change. It may have been an accidental name, by which he was known to his intimate friends or in early life, but dropped later when he achieved reputation and literary renown, the other three containing all that a Roman patrician required.³⁴

I have examined a great many editions, lives, translations, etc., of Horace with reference to this theory, and have found it mentioned but once³⁵ and then with disapproval. It seems to have been first brought forward and championed by Bianconi, an Italian author, in 1779.³⁶ I have not been able to find Bianconi's work in the libraries here and have therefore not been able to avail myself of his arguments. Targa, the author of the best text of Celsus,³⁷ and Sprengel in his great history of Medicine,³⁸ both agree with him.

Finally, a possible explanation of "*Albinovanus*" is found in a German translation of the Epistles of Horace by Carl Passow, Leipzig, 1833. He translates Celsus Albinovanus, "*C. of Albinova*," thus implying that this term indicated the place of his birth or residence. This would assimilate it still closer to the accidental cognomina, to which I have referred. I have met with this explanation nowhere else, and I have not been able to find any such place as *Albinova* in any of the geographical dictionaries, but it appears both plausible and reasonable. The termination "*anus*" would

³⁴ Orelli regards "*Albinovanus*" as an "*agnomen*;" 3d ed. (Baiterus), 1852.

³⁵ Orellius, *op. cit.*

³⁶ Bianconi, *Lettere sopra A. Cornel. Celso*, Rom, 1779, 8°, deutsch von S. Ch. Krause, Leipz., 1781.

³⁷ Targa, Leonard, 1st ed., Padua, 1769; 2d, 1810; 3d, 1815.

³⁸ Sprengel (French trans., Paris, 1815, 9 vols.) says "infinitely probable." Targa devoted 70 years to the study of Celsus; all authors since his day have adopted his text.

²⁸ *Celsus*, Praefatio.

²⁹ Sat. II, 5, 32.

³⁰ Epist. II, 2, 10.

³¹ Sat. II, 3, 25.

³² Sat. II, 2, 56.

³³ Sat. I, 3, 58.

^{33a} Epist. I, 13, 8.

^{33b} Sic. & Liv.

correspond with Romanus, Trojanus, Albanus, etc., and the name Albinovanus certainly suggests place, "albi" or "albia nova." There were several towns of the name albi or albia, and there was an Alba Longa, an Albamarla, an Albamala, an Albamana, and many similar combinations. The termination "anus" indicates a double word since the adjective termination of polysyllables was not "anus" but "ensis."

It is pleasant, thus, to contemplate Horace as the friend of our Roman Hippocrates, and I feel sure that the works of the genial poet will afford us increased delight from the contemplation of this tie between our profession and him.

The following diseases are mentioned in Horace: dropsy, *dirus hydrops*; consumption, *macies*; malaria, *quotidiana*, *quartana frigida*; fever, *febris*; pleurisy, *dolor laterum*, *dolor miseri lateris*, *morbus lateris acutus*; *polypus nasi*; headache, *dolor capitis*; dyspepsia, *dolor cordis*; lethargy, *lethargus*, *reternus*; insanity, *iracunda Diana*, *furor*, *insania*, *rabies*; ulcer, *ulcus*, *ulcera incurata*; hydrophobia, *rabies canis*, *rabiosa canis*; diabetes [if the lines

"Si tibi nulla sitim finiret eopia lymphæ,
Narrares medicis;"

justify this diagnosis]; wound, *vulnus*; itch, *scabies*; jaundice, *morbus regius*; cold, *frigus*; conjunctivitis, *lippitudo*; strabismus, *strabo*; club-foot, *male pravae tales*, *crura distorta*; wart, *verruca*; protuberance, *tuber*; a horny growth on the forehead, *frons exsecto cornu*; fracture of the leg, *crus fractum*; Campanian disease, *morbus Campanus* [a skin eruption accompanied by pimples or warts]; mole, *nævus*; gout, *nodosa* (knotty) *chiragra*, *tarda* (crippling) *podagra*; cough, *tussis*; wax in the ear, *auriculæ dolentes collecta sorde*; plague, *pestis*; canities, and bites of dogs and serpents.

The allusion to dropsy is strikingly graphic: As the love of money increases with its gratification, so "the direful dropsy increases by self-indulgence, nor does it extinguish its thirst, unless the cause of the disease has departed from the veins, and the watery languor from the pallid body."³⁹ There is an allusion to this affection also in Epist. I, 2, 34: "*Si noles sanus, curres hydropicus*," "although you are unwilling to move when well, you will run fast enough" [to the doctor], "when you get the dropsy." The origin of consumption and fevers, as a retribution for the theft of fire from heaven by Prometheus, is strikingly put—

"macies, et nova febrium
Terris ineubuit cohors,"⁴⁰

as if they were swarms of noxious winged creatures. The polypus of the nose,⁴¹ resembled more ozæna, from the fetid odor which accompanied it, than what we know as polypus. The word scabies occurs three times. "*Occupet extremum scabies*,"⁴² "the devil take the hindmost!" The jaundice is called "*morbus regius*," not because like serofula in later times, it was curable by the king's touch, but because, in its treatment, it required care and delicacies which are supposed

to be attainable only by royal personages.⁴³ *Colligere frigus* "is "to catch cold"; *tentatus frigore*⁴⁵ is "seized with a cold." "*Hic oculis ego nigra meis collyria lippus illinere*,"⁴⁶ "here I anointed my inflamed eyes with black ointment." What this black ointment was is not stated in any of the commentaries; Celsus gives the formulæ for several, among which this may possibly be. Again we have "*lippus inungi*,"⁴⁷ "*Crispinus lippus*,"⁴⁸ and "*oculis lippus inunctis*."⁴⁹ The crippling effects of gout are portrayed at Sat. II, 7, 14: "That buffoon Volanerius, when the deserved gout had crippled his fingers, maintained a fellow, hired by the day, to take up the dice and put them into a box for him." The removal of the horny growth from the forehead of Messius, spoken of in the description of the journey to Brundisium,⁵⁰ was doubtless effected by some surgeon; an ugly scar attested the operation. The Cæsarean operation is clearly referred to in the *De Arte Poet.*, 339: "Nor take out of a witch's belly" [*alvo*], "a living child, that she had dined upon." In Sat. II, 3, we have a discussion of insanity, with a description of various types. It enumerates many well-known forms but omits others. There is no mention, *e. g.*, of general paralysis of the insane (referred to by Pliny), nor of alcoholic, puerperal or epileptic insanity. Although but a desultory description, it is worth a closer study.

In Horace's physiology, the liver secreted bile as now, but figuratively it was also the seat of anger and lust.

"meum
Fervens difficili bile tumet jecur,"⁵¹

"My inflamed liver swells with bile difficult to be repressed."

"libido
Saeviet circa jecur ulcerosum,"⁵²

"And hot lust shall rage about your ulcerous liver." "*Non ancilla tuum jecur ulceret ulla*,"⁵³ "let no young slave inflame your liver." "*Meum jecur urere bilis*,"⁵⁴ "anger galled my liver" [because his dear friend Fuscus Aristius would not take the hint, when he was tormented by the bore on the Via Sacra].

"Exucta uti medulla et aridum jecur
Amoris esset poculum,"⁵⁵

"that they" [the witches] "might have a love-filter from the parched marrow and dried liver" [of the boy]. At Od. IV, 1, 12, the poet advises Venus to seek Paulus Maximus, "if she desires to inflame a suitable liver:" "*si torrere jecur quæris idoneum*." In Od. III, 4, 77,

"nee Tityi jecur
Relinquit ales,"

"the vulture feeds continually on the liver of Tityus" [the giant, who had attempted violence upon Latona]. And finally, we find this mention of the bile in Sat. II, 2, 75:

"Dulcia se in bilem vertent, stomachoque tumultum
Lenta feret pituita,"

⁴³ See Celsus, lib. III, 24. ⁴⁷ Epist. I, 1, 29.

⁴⁴ Epist. I, 2, 13.

⁴⁵ Sat. I, 1, 80.

⁴⁶ Sat. I, 5, 30.

⁴⁸ Sat. I, 1, 120.

⁴⁹ Sat. I, 3, 25.

⁵⁰ Sat. I, 5, 58.

⁵¹ Od. I, 13, 3.

⁵² Od. I, 25, 15.

⁵³ Epist. I, 18, 72.

⁵⁴ Sat. I, 9, 66.

⁵⁵ Epod. V, 37.

³⁹ Od. II, 2, 13. ⁴⁰ Od. I, 3, 30. ⁴¹ Epod. XII, 5.

⁴² De Arte Poet.

which Martin translates—

“ what tasted so sweet
Will be turned into bile, and ferment, not digest, in
Your stomach, exciting a tumult intestine.”

The spleen is not once mentioned, and with Horace it was “to vent the bile,” not “the spleen.”

Cor is used for heart or stomach, *præcordia* for heart, chest or intestines. *Ilia* is also used in the last-named signification. “*Vitio tumidum cor*,”⁵⁶ “heart swollen with vice”; “*tetigisse cor querela*,”⁵⁷ “to move the heart with complaint”; “*corde tremit*,”⁵⁸ “trembles in her heart”; “*in cor trajecto dolore*,”⁵⁹ “the pain being transferred to the stomach.” “*Ilia rhombi*,”⁶⁰ “the entrails of a turbot”; “*O dura messorum ilia*,”⁶¹ said of those who eat garlic; *ducere ilia*,”⁶² “to become broken-winded.” “*Humana exta*”⁶³ is “human viscera.” “*Tenta spiritu præcordia*,”⁶⁴ “my chest strained with gasping”; “*condita cum verax aperit præcordia Liber*,”⁶⁵ “when truth-telling Bacchus opens the secrets of his heart”;

“ leni præcordia mulso
Prolueris melius,”⁶⁶

“you will with more propriety wash your stomach with soft mead”; “*quid hoc veneni saevit in præcordiis*,”⁶⁷ “what poison is this that rages in my entrails?” [said of the garlic]; “*et inquietis assidens præcordiis*,”⁶⁸ “and brooding upon your restless breasts”; “*inæstuit præcordiis*,”⁶⁹ “boils in my breast.”

The lungs are not mentioned once, and the medulla [besides the quotation already given] only in this passage: “*certius accipiet damnum propiusve medullis*,”⁷⁰ “and nearer to his marrow.”

Disease of the nerves is referred to once only,⁷¹ but “*nervi*” is to be understood rather as signifying tendons and muscles than nerves. “*Cerebrum*” is used for brain or head: “*truncus illapsus cerebro*,”⁷² “*felix cerebri*,”⁷³ “*putidius multo cerebrum*,”⁷⁴ “*Cerebrosus*”⁷⁵ indicates “a choleric fellow.”

“Foul lust” inflames the veins⁷⁶ as well as the liver. Wine flows into the veins.⁷⁷ The cause of disease resides in the veins.⁷⁸ “To commit to the empty veins.”⁷⁹ There is no mention of the arteries (Celsus uses “*venæ*” as a general term for both).

“*Venter*” is used almost always for the organ of digestion, but in Epod. XVIII, 50, it signifies the womb, and in Epist. I, 15, 36 the abdomen, “*urere ventrem*,” “to brand the abdomen.” “*Stomachus*” also generally implies the organ of digestion, but once it is used to signify “anger,” once “breast” and once “disposition.”

⁵⁶ Sat. II, 3, 213.

⁵⁷ De Arte Poet., 98.

⁵⁸ Od. I, 23, 8.

⁵⁹ Sat. II, 3, 28.

⁶⁰ Sat. II, 8, 30.

⁶¹ Epist. III, 3, 4.

⁶² Epist. I, 1, 9.

⁶³ De Arte Poet., 186.

⁶⁴ Epod. I, 18, 25.

⁶⁵ Sat. I, 4, 89.

⁶⁶ Sat. II, 4, 26.

⁶⁷ Epod. III, 5.

⁶⁸ Epod. V, 95.

⁶⁹ Epod. II, 15.

⁷⁰ Epist. I, 10, 28.

⁷¹ Epist. I, 15, 6.

⁷² Od. II, 17, 27.

⁷³ Sat. I, 9, 11.

⁷⁴ Sat. II, 3, 75.

⁷⁵ Sat. I, 5, 21.

⁷⁶ Sat. I, 2, 33.

⁷⁷ Epist. I, 15, 18.

⁷⁸ Od. II, 2, 14.

⁷⁹ Sat. II, 4, 25.

“*Guttur frangere*”⁸⁰ is to break one’s neck; “*cervicem frangere*”⁸¹ is used in the same sense.

The midwife is referred to once:

“ et tuo
Cruore rubros obstetrix pannos lavit,
Utcunque fortis exsiliis puerpera,”⁸²

“and the midwife washes the rags, red with your blood, as often as you bring forth, springing up with unabated vigor.” This is said in derision of Canidia the witch. “*Laudantur simili prole puerperæ*,”⁸³ “mothers are praised for the resemblance of their offspring,” an allusion to the blessings Augustus had conferred upon his country.

“ Diana, quae laborantes utero puellas,
Ter vocata, audis, adimisque letho,”⁸⁴

“Diana, who when thrice called, hearest young women in the throes of childbirth and snatchest them from death.”

Constipation is referred to in the words, “*dura morabitur alvus*.”⁸⁵

Horace’s materia medica is singularly limited. Of drugs he mentions the following only: “*malva*,”⁸⁶ mallows; “*lapathum*,”⁸⁷ sorrell; “*elleborum*,”⁸⁸ hellebore; “*abrotanum*,”⁸⁹ southernwood; “*cicuta*,”⁹⁰ hemlock; “*papaver*,”⁹¹ poppy.

The mallow was used for food and also as a remedy for various disorders, as indigestion, irritation of the kidney and bladder, etc.: “*gravi malvæ salubres corpori*.”⁹² Celsus recommends it frequently as an emollient and laxative.

There were two varieties—the cultivated, *sativa*, and the wild, *silvestris*. The mallow (“*althæa*”) is still employed in medicine as a demulcent and emollient. The root of the plant which grows in salt marshes and other moist places is alone officinal. It is obtained from Europe.

The sorrel, known among the Greeks as “*lapathon*” and among the Romans as “*rumex*,” grows also in swamps. It was described by Pliny and Dioscorides, according to the latter being stomachic, laxative and diuretic. Celsus recommends it as a laxative. It is still embraced in our materia medica, having an agreeable sour taste (due to acid oxalate of potassium) and valuable antiscorbutic properties.

Hellebore was in great repute in the treatment of insanity. According to Pliny,⁹³ it will cure paralysis of the insane (“*paralyticus insaniens*”), expelling bile, feces and mucus and with these “the melancholy humor.” The same author states that the illustrious tribune, Drusus, was cured by it of epilepsy. Celsus does not mention it. The plant was found in great abundance on the island of Anticyra, in the Aegean Sea, and thither wealthy patients with mental disorders were sent to undergo courses of treatment with it. Hellebore (known as “*Helleborus Orientalis*”) is still found growing in the Island of Anticyra. It is distinct from the black hellebore, which is also found in Greece, though probably possessing similar properties.

⁸⁰ Epod. III, 2.

⁸¹ Od. II, 13, 6.

⁸² Od. I, 31, 16; Epod. II, 58.

⁸³ Sat. II, 4, 29; Epod. II, 57.

⁸⁴ Epod. III, 3; Sat. II, 1, 56; Epist. II, 2, 53.

⁸⁵ De Arte Poet., 375.

⁸⁶ Epod. XVII, 50.

⁸⁷ Od. IV, 5, 23.

⁸⁸ Sat. II, 3, 82; Epist. II, 2, 137.

⁸⁹ Epist. II, 1, 114.

⁹⁰ Epod. II, 57.

⁹¹ Lib. XXV, ch. 15.

The *abrotanum* (southernwood) was an evergreen plant, of very bitter taste; both leaves and seed were employed and were considered by Pliny and others to be highly useful in diseases of the nerves, coughs, lumbago, urinary difficulties, poisoning, etc. Celsus recommends it as a diuretic in dropsy. In the last edition of the U. S. D., the leaves of *Artemisia Abrotanum*, L., or southernwood, are said to have a fragrant odor and a warm, bitter, nauseous taste and to have been formerly employed as a tonic, deobstruent and anthelmintic. It is allied to the *Artemisia Absinthium*, from which the intoxicant absinth is derived.

The *cicuta* (hemlock) was a painless poison, producing narcotism with coldness of the body. Among the Athenians, those condemned to death were compelled to drink its juice; thus perished Socrates and Phocion. It is mentioned twice by Celsus. The effects of the modern conium which is supposed to be identical with it, are anodyne, soporific and antispasmodic. "After toxic doses, the muscular prostration is extreme, the eyelids drop from weakness, the voice is suppressed, the pupils dilated, the light almost lost; consciousness is usually preserved to the last and life is finally extinguished without a struggle. . . . Probably the most frequent use of it is by alienists for the production of calm in maniacal excitement." (U. S. D.)

"*Sed mala tollet anum vitiato melle cicuta*,"⁹⁴ "the deadly hemlock in the poisoned honey will take off the old dame"; *cicutis alium nocentius*,"⁹⁵ "garlic more baneful than hemlock."

The poppy is mentioned in "*De Arte Poet.*," 375: "*Sardocum melle papaver*," "the poppy mixed with Sardinian honey," rendering it very bitter and therefore cheap. The papaver, both "*album*" and "*nigrum*" is often spoken of by Celsus in connection with its hypnotic effects.

"*Fomenta*," both hot and cold are mentioned: "*Fomenta vulnus nil malum levantia*,"⁹⁶ "applications that give no ease to the desperate wound"; "*fomenta parare*,"⁹⁷ "*frigida curarum fomenta*,"⁹⁸ "the cold fomentations of care." In Epist. I, 2, 52, fomentations are said to be "as useful to the gout as paintings to the blind or music to the deaf," from which we may infer that they were not in much esteem in that disease.

⁹⁴ Sat. II, 1, 56.⁹⁶ Epod. XI, 17.⁹⁸ Epist. I, 3, 26.⁹⁵ Epod. III, 3.⁹⁷ Sat. I, 1, 82.

Baths, cold, hot and sulphur, are frequently referred to. It is well known how large a part they took in Roman life, both in health and disease. It is singular that there is no mention of blood letting or cups which were then in frequent use. The leech (first recommended by Themison, Horace's contemporary) is mentioned once and is the very last word in the book:

"*Non missura cutem, nisi plena cruoris, hirudo*," "a leech that will not quit the skin till saturated with blood"; this is said of the "*recitator acerbus*," "the merciless reciter of verses," "the mad poet." It is not mentioned by Celsus.

There are several allusions to the unhealthfulness of the autumn season at Rome; "the sickly hours of September"; "the sickly season of autumn";¹⁰⁰ "the undertaker with his black attendants, active in autumn,"¹⁰¹ or as Martin interprets it:

"this deadly time of year,
When autumn's clammy heat and deadly fruits,
Deek undertakers out and inky mutes;
When young mammas, and fathers to a man,
With terrors for their sons and heirs are wan,
When stifling anteroom or court distills
Fevers wholesale, and breaks the seal of wills."

Again

"the southern breeze
That through the autumn hours wafts pestilence and bale."¹⁰²

From line 302, *De Arte Poet.*, there would seem to have been a custom among certain of the Romans of submitting to an annual vernal purgation:

"O ego laevus
Qui purgor bilem sub verni temporis horam."

In Epod. XVIII, 35, Horace calls the witch Canidia, a shop or laboratory of poisons, "*venenis officina Colchicis*," just as we now say a man is "an encyclopædia of knowledge."

In Sat. II, 5, 7, Ulysses finds neither his "*apotheca*," i. e., "cellar" or "storehouse," nor his flock, untouched by the suitors of Penelope.

Among those who grieve over the death of the singer, Tigellius, are the "*pharmacopolæ*,"¹⁰³ a term which Smart says was a general appellation for all dealing in spices, essences and perfumes. It is probable that they also dispensed drugs to the poorer classes.

⁹⁹ Epist. I, 16, 16.¹⁰¹ Epist. I, 7, 6.¹⁰³ Sat. I, 2, 1.¹⁰⁰ Sat. II, 6, 19.¹⁰² Martin, Od. II, 14, 15.

A HISTORICAL NOTE UPON DIPTERA AS CARRIERS OF DISEASES—PARÉ—DÉCLAT.

BY HOWARD A. KELLY, M. D.

(Read before the Johns Hopkins Hospital Historical Club, Monday, March 11, 1901.)

It is with no little sense of satisfaction that the surgeon contemplates the recent enormous advance so unexpectedly made in the direction of hygiene and preventive medicine, an advance of even greater significance I am inclined to think than the discovery of Jenner, and one which is fairly

comparable to the introduction of the antiseptic principle into surgery.

It is a curious fact that our greatest acquisitions sometimes steal upon us so silently and so unheralded that before we know that any change has occurred a new principle has

been quietly evolved, and we find ourselves in possession of facts destined within a few years to save millions of lives and a vast sum of morbidity, where life is not lost. Such too is the case with this recent greatest medical discovery of the significance of the diptera and other insects as intermediary hosts and conveyers of contagion.

The interest in the subject which has been aroused in this country can be inferred from these admirable monographs and papers, some of which I here present to the Society:

Geo. H. F. Nuttall, On the Rôle of Insects, Archnids and Myriapods as Carriers in the Spread of Bacterial and Parasitic Diseases of Man and Animals. The Johns Hopkins Hospital Reports, Baltimore, 1899.

Victor C. Vaughan, Conclusions reached after a Study of Typhoid Fever among the American Soldiers in 1898. Jour. Am. Med. Assoc., June 9, 1900.

Geo. M. Kober, Report on the Prevalence of Typhoid Fever in the District of Columbia, published in the Health Officer's Report for 1895. I have to thank Dr. Kober for this manuscript copy of his investigations.

Walter Reed, The Etiology of Yellow Fever. Jour. Am. Med. Assoc., Feb. 16, 1901.

Charles Finlay, The Mosquito Theory of the Transmission of Yellow Fever, with Its New Developments. Medical Record, Jan. 19, 1901.

L. O. Howard in the Proceedings of the Washington Academy of Sciences presents most valuable data in "A Contribution to the Study of the Insect Fauna of Human Excrement," Washington, 1900; Dr. Howard collected 77 species of diptera, of which 36 species were found to breed in human excrement. The commoner and more important forms can easily be identified by means of the admirable figures scattered through the text.

Previous to this article no systematic attempts had been made to identify the species, all of which were simply spoken of generically as "flies."

L. O. Howard, Ph. D., remarks that in general there may be said to be three predominant types of flies, the medium-sized gray, of the type of the common house fly (*Musca domestica*), the metallic green and blue bottle flies, and the small dark brown or black flies of the *Homalomyia* type.

Several species belonging to the different families so closely resemble the house fly that they cannot be distinguished without a close study of structural characters.

I know myself by questioning friends during many past summers that few laymen even recognize the difference between the common house fly and the gray horse fly of the same size (*Stomoxys calcitrans*) with his prominent biting proboscis.

The importance of the recognition of specific differences is manifest when we come to study the life history of flies with a view to extermination.

An instructive article for the lay scientific world by Dr. Howard will be found in the Popular Science Monthly for Jan., 1901.

My object in presenting this matter to the Society this

evening is, however, not to review a subject already very large but simply to present two brief historical notes which I think have as yet escaped the attention of any writer. I am glad that my little historical investigations in both instances serve to illuminate the great genius of our French confreres and add but another to the many instances in which they have been shown to lead the world in the field of science.

The first clear statement as to any definite relationship existing between flies and disease as that of cause and effect is found in the works of Ambroise Paré in his "Apologie, et Traité contenant les Voyages Faits en Divers Lieux," where he describes how after the battle of St. Quentin (1557) he was sent by the king to la Fere in Tartenois. Arriving at la Fere, Paré was charged as he was about to return by M. le Mareschal de Bourdillon to remain and dress the wounded survivors of the battle, "which," as he tersely says, "I did" ("ce que je fis").

He found the wounds excessively fetid and full of worms with gangrene and corruption; and it was necessary to give free play to the amputating knives in removing the decay in cutting off arms and legs; there were also sundry trephinnings. To stop the gangrene and kill the worms he washed the wounds with Egyptianum dissolved in wine and brandy, but in spite of all his cares a great number died.

Now there were at la Fere some gentlemen charged with the business of finding the dead body of M. de Bois-Dauphin the elder, who had been killed in the battle, and they begged Paré to assist them in their search, but it was impossible to recognize him as the bodies were all so far gone in corruption and the faces so disfigured. "For more than half a league around, the earth was covered with dead bodies, and we could hardly stop there on account of the terrible cadaverous odor which they exhaled, men as well as horses: we were too the cause of a rising up from the bodies of a great number of large flies gendered by the moisture of the bodies and the heat of the sun; they had green and blue bellies and when they were in the air they cast a shadow on the sun. It was wonderful to hear them buzzing and wherever they settled they made the air pestilent and there they caused the pest."

Verbatim: "Nous fusmes cause de faire eslever de ces corps une si grande quantité de grosses mouches, qui s'estoient procréées de l'humidité des corps morts et de la chaleur du Soleil, ayans le cul verd et bleu, qu'estans en l'air faisoient ombre au Soleil. On les oyoit bourdonner à grand merueille, et croy qua là on ils s'assirent, c'estoit pour rendre l'air pestilent, et y cause la peste."

The value and completeness of the observation of this great surgeon is fully appreciated when we consider how short a step it is necessary to take in order to make a practical application in the prevention of the infection thus distributed by flies, whether by inhumation or incineration of the dead bodies or by the use of screens to protect the living.

What benefits might not have accrued to humanity during the past two and a half centuries had some inquiring mind

gone to work to submit this magisterial dictum to a few simple practical tests!

In the year 1668, after a severe visitation of the plague a distinguished natural philosopher, a Jesuit priest named Athanasius Kircher (*Scrutinium physico-medicum Contagiosae Luis, quae Pestis dicitur etc.* Romae 1658, p. 145), in writing of the causes of the plague—"De mirandis contagii sive fomitis pestiferi effectibus, et quaenam res contagii capaces sint," says under the remarkable caption "*muscae pestis Seminatives*," including bees as well as diptera under the title "*musca*," "Last of all flies according to Mercurialis, saturated with the juice of the dead or of the diseased then visit neighboring houses and infect the food with their filth. A hornet lit on the nose of a certain nobleman in the late Neapolitan plague, who was looking out of the window, and stung him and in two days he was dead."

My next claimant for honors is also a Frenchman, G. Déclat, a man of great ability born both too early and too late, too late to be recognized as the discoverer of antisepsis, for that honor belongs to his quondam friend and competitor Lemaire, but too early for recognition of his merits by the world at large, for his work still had to await another generation to find suitable recognition and approval.

Déclat writes, in his work entitled "*Nouvelles Applications de l'Acide Phénique en Médecine et en Chirurgie aux Affections Occasionnées par les Microphytes—les Microzoaires—les Virus, les Ferments*," etc., Paris, Oct., 1865:

"De l'acide Phénique dans les cas d'empoisonnements transmis par les insectes.

Dans notre climat nous n'avons pas de mouches réellement venimeuses, c'est-à-dire qu'une piqûre de mouche seule ne suffit pas pour amener des accidents graves, quelle que soit la partie du corps qu'elle pique. Ainsi, la piqûre des abeilles, des guêpes, des frelons ne peut entraîner que la douleur ou un peu d'enflure plus ou moins considérable, selon la nature des tissus atteints par l'insecte. Mais si la mouche n'occasionne pas d'accidents graves par sa piqûre proprement dite, elle peut cependant être la cause indirecte de désordres qui entraînent quelquefois la mort.

L'explication en est facile, et c'est cette explication qui nous donnera la clef des moyens propres à nous en préserver:

Les mouches touchent à tous les corps et de préférence aux corps végétaux ou animaux qui sont en décomposition. Or, la décomposition n'est autre chose que la désorganisation par les ferments, par ces êtres microscopiques, dont le but dans la nature est de détruire tout ce qui a vécu, tout ce qui vit et tout ce qui vivra. La mouche transporte souvent, au moyen de ses pattes, de ses ailes, de sa trompe ou de ses mandibules une quantité plus ou moins grande de ces êtres destructeurs. Si elle se pose sur un être vivant, et que la partie de son corps empreinte du virus contagieux touche la peau de cet être vivant à l'endroit d'une écorchure, quelque petite qu'elle soit, elle y dépose ce ferment, et peu à peu il pénètre à travers l'écorchure ou l'éraillure de la peau, se mêle au sang, et devient le point de départ de tous les acci-

dents auxquels donne lieu la pénétration de ces êtres dans le sang, où ils se multiplient.

Si l'ensemble de ces circonstances ne se présente pas plus souvent, on doit s'en étonner, car les mouches recherchent toujours les parties dénudées de notre corps et se placent de manière à pouvoir pomper un liquide qui leur serve d'aliment; or elles le puisent dans le fond des pores, dans les parties fines de la peau, le pourtour des yeux, par exemple, et surtout dans les écorchures, dans les éraillures, les coupures, les boutons, etc. Si les accidents ne sont pas plus fréquents, c'est que la loi organique qui défend les viscères et maintient la vie, comble rapidement les fissures de la peau par la sécrétion d'une matière coagulable à l'air. Et, dès lors, la mouche, quoique se plaçant sur ces parties, y dépose bien un principe dangereux, mais par bonheur ce principe ne peut pénétrer que bien rarement.

Par une prévoyance providentielle, les mouches armées de telle sorte qu'elles peuvent attaquer la peau, sont moins portées que les autres à se nourrir de matières septiques; sans cela, comme elles font elles-mêmes une porte d'entrée, soit avec un aiguillon, soit avec des mandibules, elles feraient pénétrer avec leur venin le germe des infusoires mille fois plus dangereux que ce qu'elles peuvent déposer elles-mêmes.

Le danger réel vient donc surtout du contact des mouches qui ne piquent pas, et cela parce qu'on ignore ce danger qui nous menace et qu'on ne le soupçonne qu'après les premiers symptômes de gonflement, de malaises ou des maux de cœur, et quelquefois il est déjà trop tard, comme cela arrive si souvent dans la *pustule maligne*. Par quel moyen donc se préserver de ce danger qui est réel?

Le premier et le meilleur serait de ne jamais laisser à l'air libre un corps en décomposition, d'enterrer toujours assez profondément les cadavres des animaux, surtout lorsqu'ils sont morts de maladies douteuses, de ne jamais les jeter dans les rivières, dans les fleuves et encore moins dans les eaux stagnantes; le second est d'avoir toujours chez soi et encore mieux sur soi, pendant l'été, un flacon d'acide phénique. L'action de cet acide est précieuse et rapide dans ces circonstances: comme preuve, je citerai une observation que j'ai recueillie tout récemment."

What could be clearer than these simple lines? All that is wanting is the vigorous scientific experiment to prove the absolute correctness of the observations for he says:

a. The fly visits bodies in process of decomposition.

b. Decomposition is nothing more or less than destruction by ferments which are living microscopic structures.

c. The fly transports on its feet, its wings, its proboscis, or its mandibles, some of these destructive agents.

d. This material is carried to and deposited upon the living body, where, if there is any abrasion, or fissures or any solution of continuity whatever, the contagious virus does its work by entering the vascular system and multiplying indefinitely.

What more could one ask? Perhaps the recognition of the different species of microorganisms and a few modern experiments to prove the thesis. But one must leave at least a little ground for subsequent workers to cultivate!

THE FIFTIETH ANNIVERSARY OF THE INVENTION OF THE OPHTHALMOSCOPE.

BY HARRY FRIEDENWALD, A. B., M. D.

(Read before the Historical Club of the Johns Hopkins Hospital, March 11, 1901.)

It is just 50 years since the ophthalmoscope* was invented. It seems proper to make reference to an event of such importance before your Historical Society and I have thought that it would interest you to spend a little time on a review of the origin and development of the instrument. It is of special interest to consider the gradual accumulation of facts and observations, the building stones which were required before even the genius of a Helmholtz could rear his structure. The most important of these was the observation of the luminous appearance of the pupil, which I dare say all of you have often seen in animals and human beings. It was easy for us to make the observation because the fact had been pointed out. But most of us are very poor observers and generations and generations of common people, of learned men, of practitioners of medicine and of ophthalmologists came and went and yet the observations bearing upon this fact stand out as a few isolated instances throughout the centuries.

The ancients observed the luminosity of the eyes of certain animals for there is doubtful mention of it by Aristotle, and Pliny says "the eyes of nocturnal animals, such as cats, are brilliant in the darkness." Similar observations were later on made in the dog, horse, sheep, weazel, hyena and the birds of prey.

The first mention of the observation in the human eye was made in 1796 by Fermin who saw that the pupils of an Ethiopian Albino were luminous. Other cases were published, as rare and curious, during the first quarter of the 19th century and some went so far as to state that the light radiating from such eyes illumined the objects on which it fell and enabled the fortunate individual to read in the dark. The bright yellow appearance of the pupils in certain forms of disease, first mentioned by Scarpa in 1816, was classically described by Beer in 1817 under the title of "Amaurotic Cat's Eye."

We find no mention of luminosity in other than albinotic or diseased eyes until 1837 when Behr observed it in a case of total iriderimia and it was not until the forties before the observation was made on normal eyes.

It is interesting to learn the theories that were offered to explain these observations. First it was regarded as a phenomenon of phosphorescence, by some as the light absorbed during the day and given off at night and later by others as the result of an internal activity similar to that of the fire-fly. It was described as varying with the seasons, with the age of the individual and with his nervous state. Electricity was also called upon to assist in explaining the luminosity of the eye. It was the "naked electricity emitted by the retina, for nowhere in the animal organism is the brain substance exposed to the naked eye as clearly as in the open interior of the eyeball" (Pallas, 1811).

But Prevost in 1818 pointed out the true cause—the reflection of the light which entered the eye, and Gruithuisen about the same time came to a similar conclusion. In 1821 Rudolphi added the observation that success of the experiment depended upon having the light thrown in, in a definite direction and that the eyes of the decapitated head of a cat were as easily made luminous as in the living.

Esser in 1826 showed that such eyes show even brighter than the living because of the larger size of the pupil, and Johannes Mueller reached a similar conclusion. In 1836 Hasenstein showed that he could make the pupil luminous by compressing the eyeball in its anteroposterior diameter, and in 1845 Bruecke gave the correct explanation of the red color of the luminous pupil in that the light was reflected by the choroidal blood-vessels.

In the following year a most important communication by Cumming in *Med. Chir. Trans.* was made. He showed that every healthy human eye can be made luminous. The person is placed at a definite distance from a light, this distance varying with the intensity of the light and the observer places himself close to the straight line between the course of light and the eye examined. He showed that the luminosity of the pupil varied with the intensity and the distance of the light and that when the distance was decreased to a few inches it vanished because the light is cut off by the head. He reported a number of cases, in one of which only could he not produce the luminous appearance. In this case the pupils were very small. It was Cumming who first suggested and used this method for examination of the posterior portion of the eyeball, making the endeavor to draw conclusions concerning the retina as well as the media from the conditions of the reflex.

About this time Bruecke's attention was directed to this subject by accidentally observing a young man's eyes become luminous, and in 1847 he invented independently the same method as that of Cumming. He also mentioned an observation of Erlach that eyes could be made luminous by the bright light reflected from his concave spherical spectacle glasses, a fact which Bruecke substantiated by experiments with others.

To return a moment to another aspect I must point out that as early as 1704 Mery observed that the fundus of cats' eyes became distinctly visible when the animal was placed under the water. La Hire explained this phenomenon five years later: "When a normal eye is in the air the rays of light issuing from a point in the fundus are so refracted that they leave the eye in parallel lines. For this reason we should be able to see the point in the fundus clearly, for parallel or almost parallel rays always produce a distinct perception in our eye; nevertheless, we do not see the object. On the other hand, when the eye is under water the

rays leaving the eyeball diverge and in passing from the water into the air they are made to diverge still more. The result is that wherever we place our eye these divergent rays give us a clear picture of the point in the fundus from which they emerge." He does not attempt to explain the problem why the parallel rays emerging from an eye exposed to the air cannot be seen.

La Hire's profound statement was too advanced, others receded from it and it required almost 150 years before the problem was solved.

In 1851 a little pamphlet was published by Helmholtz, then a young professor of anatomy and physiology in Königsberg, under the title of "*Beschreibung Eines Augenspiegels zur Untersuchung der Netzhaut im Lebenden Auge.*"¹ In this he demonstrated the fundamental fact that the rays pass out of the eye in the same lines in which they have entered. He explains Cumming's and Bruecke's observations as being due to the fact that the eye is not exact focus for the light and thus rays pass out by lateral dispersion. But what was most important, he added the *practical* to the *theoretical* and described an instrument with which the details of the retina could be examined. He described the ophthalmoscopic appearance of the retina, calculated the enlargement under which it is seen, pointed out the value of the instrument as a measure of the refraction and of the accommodative changes of the eye. He called attention to the important physiological observation that fibres of the optic nerve are insensitive to light. His short monograph was thorough and complete and gave into our hands a means of examination of which no one had yet dreamed.

In his modest way Helmholtz thus prophesies its usefulness. "I do not doubt, judging from what can be seen of the state of the healthy retina, that it will be possible to discern all its diseased conditions, so far as these, if seated in other transparent parts, such as the cornea, would admit of diagnosis by the sense of light. Distention or varicosity of the retinal vessels will be easily perceptible. Exudations in the retinal substance or between the retina and choroid, will be seen precisely as in the cornea, by their brightness upon a dark ground. Fibrinous exudations, usually much less transparent than the ocular media will, when lying upon the fundus, considerably increase its reflection. I believe also that turbidity of the vitreous body will be determined with greatly increased ease and certainty. In brief, I do not consider it an overstrained expectation that all the morbid changes of the retina or of the vitreous body that have been found in the dead subject will admit of recognition in the living eye; an expectation that appears to promise the greatest progress in the hitherto incomplete pathology of the organ."

How peculiarly applicable are the lines of Weir Mitchell:

"How keen the wind thrill of delight
When some new sun illumines our lessening night,
And problems, dark for many a weary year,
Shine, simply answered—luminous and clear."

¹ From certain statements in Michaelis' *Life of v. Graefe* (Berlin, 1877, p. 34) it would appear that the invention was really made in 1850.

The invention of this instrument ushered in a new era in ophthalmology the most important and the most prolific era in the history of this science. The influence it has wielded upon other branches of medicine is far-reaching. It will not be out of place to tell the story of the invention of the instrument in Helmholtz's words: "I was endeavoring to explain to my pupils the emission of reflected light from the eye, a discovery made by Bruecke, who would have invented the ophthalmoscope had he only asked himself how an optical image is formed by the light returning from the eye. In his research it was not necessary to ask it, but had he asked it, he was just the man to answer it as quickly as I did and to invent the instrument. I turned the problem over and over to ascertain the simplest way in which I could demonstrate the phenomenon to my students. It was also a reminiscence of my days of medical study that ophthalmologists had great trouble in dealing with certain cases of eye disease, then known as black cataract. The first model was constructed of paste-board, eye lenses, and cover glasses used in the microscopic work. It was at first so difficult to use that I doubt if I should have persevered, unless I had felt that it must succeed; but in eight days I had the great joy of being the first who saw before him the human living retina."

Helmholtz called his instrument "*Augenspiegel*" which was at first rendered into English as "*eye speculum*." The term ophthalmoscope, as Hirschberg wittily says "was given to the *German* instrument in *France* by a *Greek*" (Anagnostakis, 1854). The name ophthalmoscope has likewise been applied to an invention of Cramer for studying the lenticular reflexes, afterward called phacoscope by Donders. You will find the term ophthalmoscopy in the older works (Himly Desmarres, Wharton-Jones) to signify the examination of the eye for the purposes of diagnosis.

Passing from the name to the instrument itself it may not be superfluous to say a few words in the way of description, for the instrument has now become very rare. You see that it consists of a little metal chamber closed in front by several plates of glass set at an angle. In the back there is a space for the insertion of spherical lenses. The instrument is adapted only for close work, for what is known as the direct method, by means of which the fundus is seen in upright image. As such it is a perfect instrument optically speaking and it has been employed for some of the best work ever done.

It is interesting to learn how the instrument was received. In Germany it immediately attracted attention. Graefe was one of the first to recognize how invaluable it would be. His biographer Michaelis tells us that "when he first saw not only the red reflex but also the individual parts of the fundus, his eyes sparkled, his cheeks became flushed and he exclaimed enthusiastically 'Helmholtz has opened a new world to us'—and then he thoughtfully added 'how much there will be to discover there.'" Arlt procured an instrument immediately but he tells us in his autobiography that he had great difficulty in mastering it. Ruete, Donders, Coecius,

Stellwag and a great number of others busied themselves with it and soon added important contributions.

In France it was likewise taken up eagerly and Lieber tells us that it was so highly thought of that a Frenchman spoke of it "as a German invention that was so beautiful that it deserved to have been made by a Frenchman."

The earliest mention that I can find in English literature is an account in the *Monthly Journal of Medical Science* in July, 1852. W. R. Sanders here describes Helmholtz's eye speculum and the Donder's Epken's modification. An excellent article appeared in October, 1854, in the *British and Foreign Medical Review*, by Wharton Jones. In this he reviews the original contribution of Helmholtz and those of Ruete, Coccius, Anagnostakis Van Trigt, and Eduard Jaeger. It is here likewise that he mentions the following interesting account: "It is but justice that I should here state however that seven years ago Mr. Babbage showed me the model of an instrument which he had contrived for the purpose of looking into the interior of the eye. It consisted of a bit of plain mirror, with the silvering scraped off at two or three small spots in the middle, fixed within a tube at such an angle that the rays of light, falling on it through an opening in the side of the tube were reflected into the eye to be observed and to which one end of the tube was directed. The observer looked through the clear spots of the mirror from the other end. This ophthalmoscope of Mr. Babbage we shall see is in principle essentially the same as those of Epkens and Donders, of Coccius and of Meyerstein, which themselves are modifications of Helmholtz."

What a pity that Babbage did not devote a little more time to this invention; he could hardly have missed being the inventor of an instrument whose value is a thousand times greater than that of all the calculating machines ever invented.

The earliest account of the ophthalmoscope in America is the review of Sanders mentioned above, and reprinted in the *American Journal of Medical Sciences*, July, 1853. One of the earliest accounts and one especially interesting to us is the report given by the committee on surgery (Drs. Christopher Johnson, Richard McSherry and Joseph Wilkins) to the Medical and Chirurgical Faculty of Maryland on June 7, 1854. The writer (probably Christopher Johnson), gives an account of the subject, far from good—but we are interested in learning that he "experimented with Helmholtz's speculum in Berlin with von Graefe, in Paris, with Desmarres, and in Baltimore, with Prof. G. W. Miltenberger." He illustrates the paper with colored drawings—which had better been left out.

Let us now take up the modifications of the instrument. The first was by Donders and Epkens in Holland in the same year, 1851, in which Helmholtz's publication appeared. The modification consisted in using a plain silvered mirror in place of the plates of glass.

As mentioned before, Helmholtz's instrument was adapted only for the upright method. In 1852 Prof. C. G. Theod. Ruete of Goettingen published a short paper in which he

described the following modification: He replaced the plates of glass as reflector by a perforated concave silvered mirror about three inches in diameter and examined the eye from a distance, placing concave and preferably convex spherical glasses before the eye examined. In this way he obtained an inverted image of the fundus and thus it was he who practically introduced the important method of examination known as the indirect method.² This method reveals the fundus much less highly magnified, but it has the advantage of giving a much larger field, and in this way it supplements the direct method in much the same way as the examination with high and low powers of the microscope supplement each other. Ruete's invention is really the only important addition that has been made to Helmholtz's method and it is therefore one which deserves special praise. Ruete described a few pathological cases examined by means of his instrument; these so far as I am aware are the first on record.

His publication called out a second paper by Helmholtz, entitled "Ueber eine Neue Einfachste Form des Augenspiegels," in *Vierordt's Archiv*, 1852, p. 827.

In this article Helmholtz thoroughly explained the optical principles upon which Ruete's method depended and then he described his simplest form of ophthalmoscopic examination which required only a candle and a strong convex lens. The observer's head is placed close to the candle but shaded from it and the lens held near the eye examined. This, and Ruete's method he showed were practically identical. He also mentioned an addition to his instrument by the celebrated instrument maker of Koenigsberg, Rekoss. The insertion of correction glasses in the old instrument was tedious and annoying. Rekoss placed two discs which had lenses in their periphery in the same instrument; by turning these the lens desired could be obtained.³ This device, the Rekoss disc, has been used in most modifications of the instrument.

In 1853 Coccius invented a modified instrument which for a time was very popular; it was von Graefe's favorite. It consisted of a plain mirror upon which the light thrown through a convex spherical glass attached to the instrument.

None of these instruments, however, equaled in usefulness the one described the following year by Eduard Jaeger. This was essentially a Helmholtz instrument in which there were two reflectors, one composed of plates of glass, like Helmholtz's, the other a concave mirror; the former was used for the direct, the latter for the indirect method of examination.

The invention of new forms of ophthalmoscopes now be-

² In his original communication Helmholtz discusses the possibility of using convex lenses and obtaining an inverted image. He used two convex lenses, one placed in the position usually taken by the concave lens in the back of the ophthalmoscope, the other at a distance which was less than the sum of the focal distances of the two lenses. The latter lens was close to the eye of the observer. This method was very impracticable and differs essentially from that of Ruete in that the mirror is placed between the collecting lens and the observed eye.

³ Each disc contained four lenses, one those from 6 in. to 9 in., the other those from 10 in. to 13 in., all concave.

came a favorite employment of ophthalmologists. As mirrors, we find the following:

1. Plates of glass as in Helmholtz's instrument.
2. Plain, concave and convex mirrors of silvered glass or of polished metal with central opening.
3. Plain and convex mirrors upon which light was thrown through convex spherical glasses.
4. Prisms.
5. Concave and convex spherical glasses, acting at the same time as correcting glass and as reflector. These were known as Heterocentric. If other reflecting surfaces could have been found they doubtless would have been used.

Next the inventive genius of ophthalmologists devised methods of combining the parts, the illuminating lens and the mirror, the mirror and the collecting lens required for the inverted method; and finally instruments were constructed in which all the parts were more or less fixed, the so-called stationary ophthalmoscopes.

Then again it was found necessary to have a greater number of correcting lenses in the ophthalmoscope, in order to measure the refraction more accurately and a legion of inventions appeared in which one, two or three Reuss discs or combinations of such discs were employed to give the requisite array of intervals. The most ingenious of these is the well-known instrument of Dr. Loring, who at one time practised in this city.

Finally, Cooper invented an endless chain of lenses to replace the Reuss disc and thus freed himself from the limitations of a wheel which could not be made very large and therefore could not contain many lenses unless they were made exceedingly small. The popular instrument of Morton is a modification of this.

The endeavor of late years has chiefly been in the direction of lighter instruments and more convenient ones.

I must not omit to note that a number of ophthalmoscopes have been constructed in which the source of light is a small electric light within the instrument. Mention should also be made of a number of ingenious methods for the determination of refraction by the inverted method. But I dare not spend any time in considering these here.

However, there is one subject, the use of the ophthalmoscope for skiascopy or the shadow test, which I dare not pass over. The phenomenon upon which it is based was first observed by Bowman, later by Cooper and was developed by Cuignet and Parent. As a method for the objective determination of refraction it is of high value.

It is hardly necessary to ask what has been accomplished by means of this invention of Helmholtz. The answer would be: All that Helmholtz prophesied and much more. What has become of that great category of diseases known as amaurosis, conditions defined by Philipp von Walther as those in which the patient saw nothing—and the doctor nothing too? In Ruete's *Lehrbuch* published in 1853 I find 37 varieties of amaurosis, few of the names are intelligible. In their place we now find the many varied diseases of the retina, of the optic nerve and of the choroid.

It was found that not only were there many varieties of retinitis, neuritis and choroiditis, as well as degenerative processes of the same tissues, but that these changes were often more or less characteristic of different constitutional and organic diseases, such as nephritis, diabetes, syphilis, etc., of leucemia, of cardiac and general vascular disease.

In consequence an important subject developed—that of the relation of ophthalmology to general medicine, and the ophthalmoscope became an instrument of great service to the student of general medicine. Then again the diseases of the optic nerve were found to have important bearings on brain and spinal cord diseases and thus we find the old amaurosis cereбрalis and the amaurosis spinalis replaced by the varieties of neuritis and of optic nerve atrophy, characteristic of tumors of the brain, of meningitis tabes dorsalis, etc. It is not surprising therefore that the ophthalmoscope became of supreme importance to the neurologist and that an enthusiastic Frenchman called the method of examination cerebrospey (Bouchut). But nothing emphasizes this statement more strongly than that one of the best works on ophthalmoscopy was written by a neurologist (Gowers).

I should like to refer to the lessons which the ophthalmoscope has taught the pathologist in the study of embolism, of thrombosis, etc., but time will not permit.

There is one point which I dare not omit: the ophthalmoscope has been the means of making examinations of the eye accurate and through its means this branch of medicine has made a great step in advance toward that ideal, the elevation of medicine to an exact science.

It is necessary also to mention that the methods of examination of other parts of the body by means of mirrors as in otoscopy, rhinoscopy, etc., likewise owe their origin to Helmholtz. It is not generally known that in his original communication he especially mentions the use of the mirror for the examination of the nose and of the drum-head.

I shall conclude with an extract from an address by Helmholtz, delivered on the occasion when the Graefe medal was awarded him by the ophthalmic society of Germany (1886). This adds lustre to the invention through the modesty with which he regarded the part he played.

“Let us suppose that up to the time of Phidias nobody has had a chisel sufficiently hard to work on marble. Up to that time they could only mould clay or carve wood. But a clever smith discovers how a chisel can be tempered. Phidias rejoices over the improved tools, fashions with them his God-like statues and manipulates the marble as no one has ever done before. He is honored and rewarded. But great geniuses are most modest just in that in which they most excel others. That very thing is so easy for them that they can hardly understand why others cannot do it. But there is always associated with high endowments a correspondingly great sensitiveness for the defects of one's own work. Thus says Phidias to the smith ‘without your aid I could have done nothing of that; the honor and glory belong to you.’ The smith can only answer: ‘But I could not have done it even with my chisels, whereas you, without my chisels

could at least have moulded your wonderful works in clay; therefore I must decline the honor and glory, if I will remain an honorable man.' But now Phidias is taken away, and there remain his friends and pupils Praxiteles, Paionios and others. They all use the chisel of the smith. The world is filled with their work and their fame. They determine to honor the memory of the deceased with a garland which he shall receive, who has done the most for the art, and in the art, of statuary. The beloved master has often praised the smith as the author of their great success and they finally decide to award the garland to him. 'Well,' answers the smith, 'I consent; you are many and among you are clever people.

I am but a single man. You assert that I singly have been of service to many of you and that many places teem with sculptors who have decked the temples with divine statues, which without the tools that I have given you, would have been very imperfectly fashioned. I must believe you, as I have never chiselled marble and I accept thankfully what you award to me, but I myself would have given my vote to Praxiteles or Paionios.'"⁴

⁴ At the conclusion of the above address a number of old ophthalmoscopes, including an original Helmholtz ophthalmoscope and a number of old publications were demonstrated.

THE FIRST NEPHRECTOMY AND THE FIRST CHOLECYSTOTOMY, WITH A SKETCH OF THE LIVES OF DOCTORS ERASTUS B. WOLCOTT AND JOHN S. BOBBS.

BY MARTIN B. TINKER, M. D.,

Assistant Resident Surgeon, The Johns Hopkins Hospital.

As a rule, men of science and letters of all nations specially delight to honor those of their own countrymen who have added noteworthy contributions to the sum of human knowledge. In medicine, particularly, we see much of this pride in national achievement. To the loyal German student of medicine nearly everything worthy of mention seems to have been accomplished by Germans; the same is true of the Englishman and of the Frenchman. The American medical profession, however, seems to be somewhat of an exception to this rule. It is true that we are still young as a nation and have not yet had time to accomplish as great results as the older nations, but decidedly too little is known about that which has been already accomplished among us. We know too little of those whose achievements in most other countries would be well known to all their countrymen. The object of this paper is to bring to your attention some facts about two pioneers in American surgery whose names and work are not as generally known and honored in the American medical profession as I believe they deserve.

The first nephrectomy was performed by Dr. Erastus B. Wolcott, of Milwaukee, June 4, 1861. I am unable to find that he ever formally reported the operation, but the following account of the facts of the case are given by Dr. Charles L. Stoddard, of E. Troy, Wisconsin, in the Philadelphia Medical and Surgical Reporter for 1861-62, Vol. VII, page 126. The title is "Case of Encephaloid Disease of the Kidney, Removal, etc." With the exception of a few unnecessary details, I quote in full:

"On the 4th of June last I was invited to assist Dr. E. B. Wolcott, of Milwaukee, in the removal of a tumor from the abdomen of Mr. J., aged 58 years. On examination we found that the patient was a tall, anæmic looking man of a peculiar cast of countenance, indicative of serious organic disease. He stated that he was of healthy parentage, and had good health until the appearance of the tumor six years before

that time. The physician in attendance stated that from the first appearance of the disease, some irritation of the urinary organs had existed, but what the deposits were we were unable to learn, as no reliable chemical or microscopical evidence was presented.

We found the tumor to be large, filling the right hypochondriac region and pressing the abdominal parietes forward about two inches from their natural level. On palpation it was evident that it was semi-solid, having a pedicular attachment, apparently to one of the sulci of the liver, with more extensive attachment to the posterior parietes.

Having no reliable data to form a diagnosis, other than the present state, after duly considering the patient's anxiety, and his deprivation of general health, we concluded that an operation offered the only chance of ultimate recovery; at the same time we stated to the patient and his friends that the operation was a serious one in his state of health. Our conclusion was, that we had here a cystic tumor of the liver, pressing on the kidney and producing irritation sufficient to account for the albuminous deposit. After the administration of chloroform, Dr. Wolcott proceeded to the removal of the tumor by making an incision diagonally across it down to the peritoneum, which we found to be very much thickened and slightly attached to it. He then proceeded to free it from its extensive posterior attachments, after which he found that the superior attachment was a very dense cord-like structure, about an inch in circumference, and apparently proceeding from the posterior part of the liver.

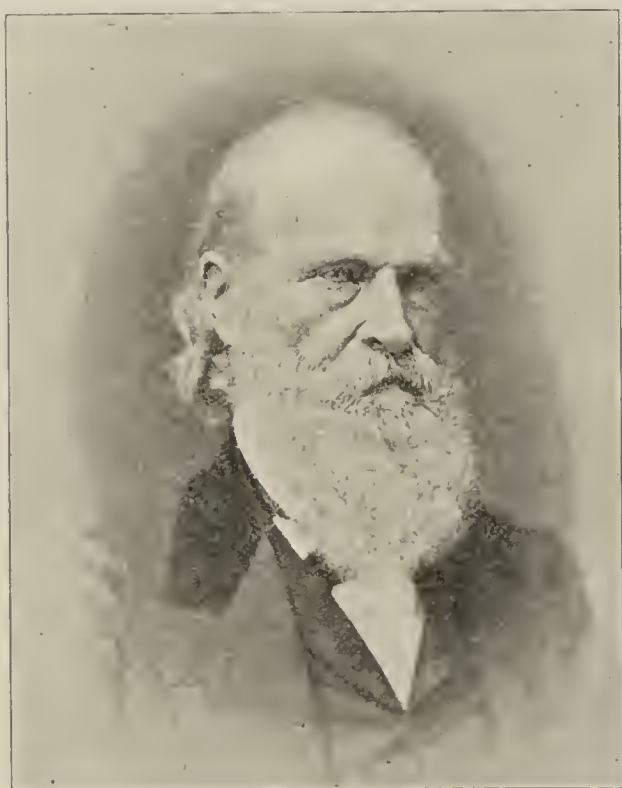
Carefully tying the pedicle, he severed this connection with a knife, and after removing foreign matter carefully from the abdomen, brought the edges of the wound together with common sutures and adhesive strips, which was the only dressing used. After the patient was free from the effects of chloroform, morphia and camphor were administered in sufficient quantities to quiet irritation and produce sleep.

The tumor weighed $2\frac{1}{2}$ pounds, and on incising it freely, we found undoubted evidence of its being a kidney from a small portion of its upper portion, which had not degenerated, showing the tubules and a portion of the pelvis.

The patient lived 15 days after the operation, and died apparently from exhaustion, caused by the great amount of suppuration which necessarily followed."

It is interesting to note that as early as the 17th century nephrectomy had been done experimentally on dogs. In an article in von Pitha and Billroth's *System of Surgery*, Heineke states that Zambeccarius in the latter part of the 17th century removed a kidney from a dog and the animal recovered. This was done after he had observed at dissections that some healthy dogs have only one kidney.

Blancard, of Amsterdam, in his "*Lexicon medicum reno-*



ERASTUS B. WOLCOTT, M. D.,

Born October 18, 1804. Died January 5, 1880.

vatum," published in 1739, also mentions experimental nephrectomy and believes that it might be performed on man.

Simon, of Heidelberg, is generally credited with having performed the first nephrectomy, but his operation, reported in *Deutsche Klinik*, Berlin, 1870, was not performed until eight years after Wolcott's operation. Simon undoubtedly deserves greater honor for having done nephrectomy experimentally on dogs, for undertaking the operation deliberately, knowing what he had to deal with and for bringing the operation before the medical profession, but the honor of priority is in no wise due to him, for Wolcott's operation was performed in 1861, more than eight years previously.

Erastus B. Wolcott was born at Benton, Yates County, New York, October 18, 1804. He was fortunate in his ancestry, coming from a race of unusually intellectual and enterprising men and women. He was the son of Elisha and Anna Hull Wolcott, who came from Litchfield County, Connecticut, and were among the first settlers of that section of

New York. The Wolcott family were from good old English stock. Henry Wolcott came to America in 1630, and his descendants in a direct line for over 180 years were among the most prominent of the colonists. Their names are found among the officers of the Colonial army, one was a signer of the Declaration of Independence, six were governors of the state of Connecticut, and there were many senators, representatives and several justices of the Supreme Court.

Dr. Wolcott's early life was like that of most children on the frontier in those days. Educational and social advantages were few, but the life of a frontiersman developed healthy bodies and minds. As a boy he attended the public schools, but I am unable to find that he had opportunities for higher education. In those days it was the custom for young men who desired to practise medicine to begin their studies with some practising physician, and Dr. Wolcott began the study of medicine and surgery with Dr. Joshua Lee, one of the most eminent men in his profession in central New York at that time. After three years' study with Dr. Lee, Dr. Wolcott received his qualification to practise medicine from the Yates County Medical Society in 1825. He was desirous of further study, and in order to earn money accepted a position as a surgeon to a mining company in South Carolina. He lived at the mines and in Charleston until 1830, when he returned to New York and attended the College of Physicians and Surgeons of the Western District of New York from 1830 to 1833, and from this institution he received the degree of Doctor of Medicine. In 1835 he took the examination for surgeon in the United States Army, and received his appointment January 1, 1836. He was stationed at Fort Mackinaw, where he met his future wife, Elizabeth J. Dousman, the daughter of a fur-trader at that post. He resigned his position in the army in 1839 and settled in Milwaukee, where he practised medicine for over forty years.

Personally, Dr. Wolcott was a man of remarkable physique. He was early noted for his great strength, and when a young man it is said that he could run and jump over a team of horses. He was also an expert shot with a rifle, shotgun or bow. His father came into the possession of an unusually strong bow once owned by the Indian chief Red Jacket. It is stated that very few white men could draw the bow to its maximum power, and not one in a thousand could use it skilfully. It is reported in the history of Yates County, New York, that Dr. Wolcott shot a blunt square-ended arrow through the siding of the first Methodist meeting-house of that county, at a distance of twenty rods. The church had been at that time abandoned. Dr. Wolcott retained his physical powers even to the time of his death. When seventy-five it is said that he could vault a five barred fence or shoot a pigeon on the wing as well as when a boy. During the last summer of his life he was called to a town at some distance to see a patient. He was desirous of reaching home as soon as possible and boarded a freight train which happened to be the first train going to Milwaukee. Finding that the train would be unavoidably delayed, he walked from the town, eighteen miles distant, to Milwaukee, and arrived some time

before the train. When he was asked why he did so he stated that he was in something of a hurry and that he wanted to see if he was really growing old.

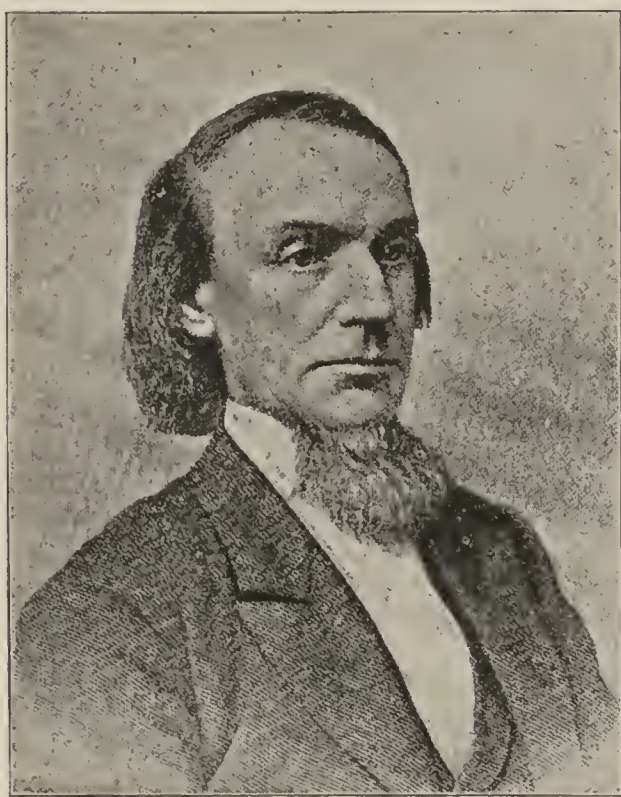
He was a man of unusual strength of character and intellectual attainments and made up for the lack of a liberal education by a wide reading. All the records which we have of him specially mention his generosity. Nothing in the way of fatigue or hardship ever prevented immediate attention to a professional call, no matter what the financial standing of the patient might be. At the time of his death thousands of poor people gathered from the city and surrounding country to honor his memory, and the arcade in which he lay in state was choked by the middle and lower classes. His great professional ability and personal popularity brought him into many public positions. He was surgeon-general of the state of Wisconsin as early as 1842, which office he held during the Civil War and to the time of his death. He was a member of the Board of Regents of the state university, a manager of the Soldiers' National Home at Milwaukee, major-general of the state militia, trustee to the Wisconsin Hospital for the Insane and commissioner to the Paris Exposition. As a consulting surgeon he was well known throughout the Northwestern states, and he was frequently called long distances in critical cases as a consultant. Dr. Wolcott's surgical achievements were not limited to performing the first nephrectomy. Among other operations which he performed and about which I have received definite personal information were: excisions of the breast, trephining, thoracotomy, an extensive plastic for the scar of burn which had fixed the chin to the chest, oöphorectomy, Caesarian section and many other major operations, some which were quite unusual in his day. It should be remembered that frontier surgeons of that day operated without the advantages of the modern, thoroughly equipped hospital, without the aid of trained assistants and not infrequently without any assistant; anti-sepsis was almost unknown and anaesthetics were just being introduced. The esteem in which he was held by his fellow citizens is shown by the fact that his funeral procession was led by six hundred veterans from the state of Wisconsin and that resolutions of sympathy were passed after his death by the Milwaukee Academy of Medicine, Milwaukee County Medical Society, and by numerous clubs and military associations. Several prominent medical men from the section in which Dr. Wolcott practiced have recently told me that they consider him the greatest surgeon the middle West has ever produced, and hundreds of people gratefully remember him as their benefactor and friend.

The first cholecystotomy was performed by John Stough Bobbs, of Indianapolis, Indiana, June 15, 1867. A report of the case may be found in the Transactions of the Indiana Medical Society for 1868. The chief features of the case are as follows:

A woman, 30 years of age, came to Dr. Bobbs in consultation with her physician. Four years previously she had noticed an enlargement in the right side which she stated was

low down in the iliac region. Her health at that time was bad. She had pain and distress on taking food or drink or after exercise, which frequently continued three or four hours. The enlargement in her side continued to increase and soon became tender. Ultimately it prevented her from walking, and following January, 1867, the increase in size was more rapid and the trouble was greater. On examination a tumor was found in the right side which was tender to pressure. Its outline could not be well made out except on the right side, where it was quite distinctly defined. The tumor was slightly movable, and the abdomen was tense and slightly projecting. Vaginal examination disclosed no connection with the uterus or its appendages. The patient was exceedingly anxious to have something done for her relief. A diagnosis of probable ovarian tumor had been made by several physicians, but after observation for a considerable time the patient was informed that the true nature of the growth was uncertain and she was given no assurance that it could be successfully removed. The patient, however, persisted in her request that an operation should be undertaken, and an exploratory celiotomy was made by Dr. Bobbs, assisted by several local physicians. Under chloroform anaesthesia an incision was made between the umbilicus and the pubes. The omentum was found thickened and adherent to the abdominal wall. It was separated toward the right side in hope of reaching some part where no adhesions existed, but failing in this, the omentum was torn through over the tumor so as to admit the finger upon the protuberant portion of it. Passing the finger around the mass some adhesions were broken up and the tumor was traced upward. No pedicle or attachment could at first be definitely made out. The abdominal incision was then carried above the umbilicus on the right side over the prominent part of the enlargement. The mass was oval in form, tense and contained pellucid fluid. An incision was made into it and perfectly clear fluid escaped with considerable force, propelling several gall-stones about the size of an ordinary rifle bullet. On introducing the finger other solid bodies were felt, but not in the main sac. A number were hooked out with the finger from this sac. They varied in size from that of a mustard-seed to that of a bullet. No communication between this sac and the main sac could be found. The second sac had the appearance externally of a hydatid cyst, its walls were of the thickness of the skin, and its inner covering was smooth and whitish. Pulling it downward the right lobe of the liver was brought into view, to the lower surface of which the sac was attached by a broad linear base like the gall-bladder. At first there was some doubt as to whether the sac was really an enlarged gall-bladder, but this seemed to be definitely identified by its form, attachments and the concretions which it contained. The sac was then closed by stitches, the nature of which is not mentioned and the abdominal wound was sutured. At a dressing one week after the operation a stitch abscess was found which had given the patient some pain and discomfort for a few days after the operation. From this time, however, the patient's recovery was uneventful.

and at the end of two weeks she was permitted to sit up, and in three weeks she was about the house. A complete report is given of the progress of the patient from day to day, but the essential points have been noted. In an editorial article which appeared in the *Indiana Medical Journal* in October, 1899, it is stated that the patient is still living near Indianapolis, thirty-two years after the operation, and in answer to a letter of inquiry from the editor of the *Indiana Medical Journal*, she writes as follows: "My gall-bladder was opened; between 40 and 50 stones were removed; there was a partition dividing one from the rest and that one was left; the size of the stones was from a shot up to a pea. I was informed that the bladder was sewed up. As to the doctors present I can remember seven, but they have all passed out but one." The names of the doctors are mentioned and the letter closes with



JOHN S. BOBBS, M. D.,

Born December 28, 1809. Died May 1, 1870.

the statement that the patient still has some trouble, which she thinks is caused by the one stone which was not removed.

John Stough Bobbs was born at Green Village, Pennsylvania, December 28, 1809. I have been unable to find very much information about his early life or education. In a memoir by Dr. P. H. Jameson, published in the *Transactions of the Indiana State Medical Society*, 1894, it is stated that Dr. Bobbs was of Pennsylvania German descent. As a child he spoke the peculiar dialect of that section. He was a man well educated in the fundamental branches, he wrote English well and was a fluent speaker. He was also well versed in history, he had a good knowledge of the English classics, and had given some attention to philosophical writings. At the age of 18 he began to read medicine with Dr. Martin Luther, of Harrisburg. After this he attended one course of medical lectures and then located in Middletown, Pennsylvania, where he prac-

tised for four years. He located in Indianapolis in 1835, but took a course of lectures in Jefferson Medical College in Philadelphia the same year, graduating in the spring of 1836 after two courses of lectures and study with a preceptor as was required in those days. He soon took high rank both as a physician and surgeon. When the Medical College of Indiana was organized he was elected professor of surgery and later dean of the faculty. As a practitioner, one of his contemporaries states that there was less sham about Dr. Bobbs than any physician he ever knew. Up to the time of his death he had never been known to give a placebo in any case and his treatment was based upon rational lines. Once when called to see a patient suffering from an acute malady, he suspended all medical treatment, giving only stimulants and foods. When questioned about his course of treatment he said: "Why give medicine here without a reason or a purpose for it?" The patient recovered and was still living and well at last accounts. Dr. Bobbs believed strongly in an organized and united medical profession and labored faithfully with that end in view. He was first in the work of establishing the Marion County Medical Society in 1847, and he was prominent in helping to organize the state society of Indiana in 1849. In both societies he was an active and prominent member. In 1868 he was elected president of the Indiana State Medical Society. His inaugural address was upon "The Necessity of a State Medical Journal and a Medical College." His paper on lithotomy of the gall-bladder, from which my report of the operation is taken, was published in the same volume of the transactions with his presidential address. The latter part of Dr. Bobbs's life was devoted mainly to surgery. He was well read in the literature of his specialty, and as an operator he was bold and original. Like most of his contemporaries, he was not a frequent contributor to medical literature. Dr. Jameson, in the paper which I have quoted, mentions an operation in which he assisted, in which Dr. Bobbs removed the superior maxillary bone together with the eye of the affected side for extensive carcinoma. The operation lasted several hours, but the patient made a good recovery. The hæmorrhage was so well controlled that little blood was lost and the patient recovered from the operation and was much more comfortable afterward. He also mentions a successful operation for extra-uterine pregnancy and an unsuccessful operation for umbilical hernia. Dr. Bobbs was a brigade surgeon during the Civil War, and in the latter office he was medical director for the district of Indiana. During the Civil War he was with the staff of General Morris, of Indianapolis, and showed his courage by bringing off the field under fire a soldier who was fatally wounded.

Besides his professional services, Dr. Bobbs was a public-spirited man who took an active part in the affairs of his city and state. For one term he served as state senator. He was one of the original commissioners who organized the Indiana Hospital for the Insane, and he gave liberally to general charitable purposes. In person he was slender, of medium height with striking features. His forehead was high, his

eyes dark grey, his nose large and aquiline, his chin prominent. He generally wore a suit of black broadcloth and a silk hat, and had the manners of the old-style gentleman.

He may be truly considered one of the founders of scientific medicine and surgery in the middle West. As the greatest general surgeon and teacher of his day in that section of the country, as a public-spirited man and soldier, his name will long be remembered in the region in which he practised.

Several others besides Bobbs did valuable pioneer work in gall-bladder surgery, but there is no evidence that I have been able to find that any one, at an earlier date, ever opened the gall-bladder after celiotomy.

Johannes Fabricius is credited with having opened the gall-bladder and removed stones from it as early as 1618. Fabricius Hildanus refers to this in his "Observations chirurgiques," published in Geneva by P. Chouët in 1669, but there is no evidence which would lead us to believe that this was an operation performed on a living person.

Among the older surgeons, Jean Louis Petit did most to clear up the symptomatology of the diseases of the biliary passages and to differentiate between these and intra-abdominal suppurative affections. In the *Memoirs de l'Academie Royal de Chirurgie*, Paris, 1743, Vol. I, p. 155, he mentioned three cases in which the gall-bladder was incised by mistake as an abscess, one of the patients recovering. From post-mortem study of several patients that died of the results of gall-bladder disease, he decided that the recovery in this case was due to adhesions to the abdominal wall. He advised lithotomy of the gall-bladder in cases in which it seemed

likely that such adhesions were present, provided the patients were extremely ill and in danger of death, but he does not mention having performed any operation which can be properly classed as a cholecystotomy. Numerous others advised and performed tapping, and several recommended abdominal section, suturing the gall-bladder to the abdominal wall and opening after several days, but no one seems to have performed the operation.

Some will be inclined to criticise the claims to the honor of priority for the two men because the operations were undertaken without a knowledge of the conditions later found. But I would like to ask, what person who has seen many operations has not seen some of the best surgeons obliged to change their diagnosis after opening the abdomen? Because Columbus set out with a purpose quite different than the discovery of a new continent, because he died without appreciating the importance of his discovery, is he any the less the discoverer of America? Both Wolcott and Bobbs were experienced surgeons, accustomed to perform all the usual major operations of the surgery of their day. Both opened the abdomen uncertain what they would meet, but perfectly understanding that the conditions they had to deal with were most grave. Both met their difficulties and coped with them successfully for the first time in the history of surgery so far as we can learn. While we concede to Simon and to Sims, Tait, Richter and Robson the honor of placing the operation of nephrectomy and the operation of cholecystotomy on a firm and scientific basis recognized and acknowledged by our profession, can we Americans afford to let the names of these two fellow-countrymen go unnoticed?

MEASUREMENT OF THE EXTERNAL URETHRAL ORIFICE.

BY G. BROWN MILLER, M. D.

The diameter of the lumen of the female urethra is given by Gray and Quain as one-fourth of an inch. Billroth and Luecke and others estimate it at 6-8 mm. So far as I can learn, no estimate based upon a large number of cases has ever been made. For the purposes of cystoscopic examination, catheterization of the ureters and the like, it is important to know what is the largest cystoscope which can be introduced without causing injury to the urethra. It has been found by Dr. H. A. Kelly that in such procedures the greatest resistance met with in the introduction of the speculum is at the external urethral orifice, and that in a normal urethra when the speculum passes this point it can be pushed into the bladder without further resistance. In dilatation of the urethra within moderate limits practically all of the laceration which occurs takes place at the meatus urinarius. It was, consequently, thought important to get accurate measurements of the diameter of the external urethral orifice. This was done in the gynecological wards of the Johns Hopkins Hospital in 100 cases. The instrument used was the urethral calibrator (Fig. 1), described by Dr. Kelly in the *American Journal of Obstetrics*, Vol. XXIX, No. 1, 1894.

The method as described by him is as follows: "I calibrate the meatus urinarius by means of a slender metal cone, which is 10 cm. long and marked in a graduated scale from the point (2 mm.) to its other end (20 mm.) in diameter. The

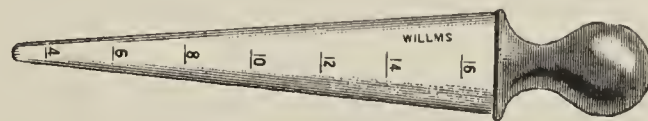
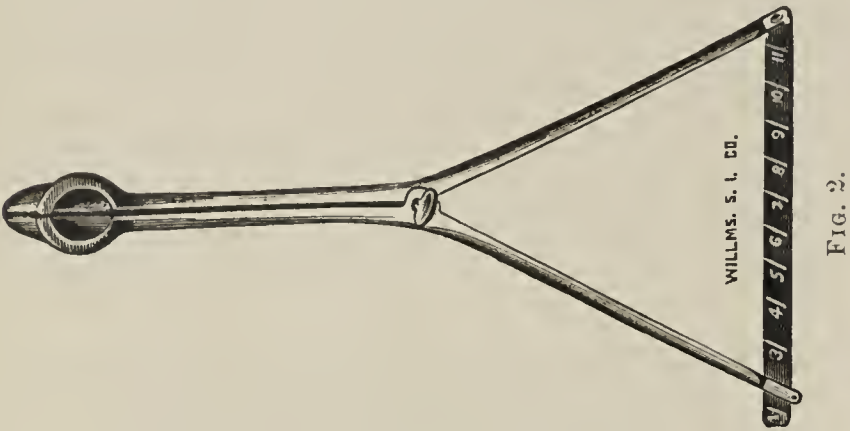


FIG. 1.

calibrator is pushed into the meatus as far as it will readily go and the marking of the meatus is noted."

I give here in a tabulated form 100 cases taken without reference to their gynecological ailment and give their age, disease, number of labors, and the measurement of the vaginal outlet. In glancing over the table one will be struck with the large number of cases operated upon for laceration of the perineum or relaxation of the vaginal outlet. This is accounted for by the fact that the measurements were taken, as a rule, only in those cases where the external genitalia had been thoroughly cleansed as preparatory to operation. In cases of abdominal section the measurements were frequently

neglected. As seen from the table, this does not, to any noticeable extent, change the average. The smallest urethral orifice (4 mm.) was found in a woman who had borne eight children and who was suffering from carcinoma of the cervix. The largest urethrae, two in number (12 mm.), were found likewise in multiparous women. While the average diameter of the external urethral orifice in nulliparous women was practically the same (7.8 mm.) as in women who had borne



children (7.6 mm.) yet in cases of extremely relaxed vaginal outlet or prolapsus of the uterus, it was found, as could have been expected, that the meatus was larger than in those cases where this relaxation did not occur.

The measurements of the vaginal orifices were made by means of the vaginal calibrator (Fig. 2), also devised by Dr. Kelly. The cut will explain the working of the instrument. It consists of two slender metal bars crossing each other and working on an axis in their middle. At one end each has a narrow curved plate and the measure is at the other end. The plates are introduced into the vagina and separated by gentle pressure, and the scale measures the diameter of the gently dilated vaginal orifice. Below is the table.

TABLE.

Age Yrs.	No. of Labors	DISEASE.	Diam. of Urethra Mm.	Meas. of Vag'al Outlet. Cm.
37	2	Prolapsus Uteri	7	6.5
36	8	Relaxed Vag. Outlet	7.5	6.5
41	3	Descensus Uteri	6	6
24	1	Relaxed Vag. Outlet	8	6.5
35	2	" " "	8	8
29	1	" " "	7	4.5
23	3	" " "	9	6
33	4	Pelvic Inflammation	6	6
35	3	Endometritis	8	6
22	1	"	8	6
35	5	Descensus Uteri	8	6
38	6	" "	9.75	7
25	0	No Gynecological Disease	8	3
..	1	Relaxed Vag. Outlet. Retrofl. Uteri	8.25	5
35	2	" " " " "	8.5	8.5
32	3	Rupture of Recto-Vaginal Septum	6	6
38	2	Relaxed Vag. Outlet	7	5
28	3	" " " Retrofl. Uteri	8	6
21	2	" " " " "	5	6
47	6	Prolapsus Uteri " "	11	7
37	7	R. V. O., Retrofl. Uteri, Ovar. Cyst.	7	6.5
23	2	Relaxed Vag. Outlet	7	6
37	3	" " " Retrofl. Uteri	6	6
32	2	Relaxed Vag. Outlet	8	6
35	8	Carcinoma Cervicis Uteri	4	..
32	6	Relaxed Vag. Outlet	12	7
32	2	Rupture of Recto. Vaginal Septum	4.5	5
34	1	Retrofl. Uteri, Relaxed Vag. Outlet	6	..
34	7	" " " " "	6	6

TABLE—Continued.

Age Yrs.	No. of Labors	DISEASE.	Diam. of Urethra Mm.	Meas. of Vag'al Outlet. Cm.
22	0	Endometritis	6	4
24	0	Retroflexio Uteri	10	..
29	4	Relaxed Vag. Outlet	8	5
30	1	" " "	8	5
26	3	" " " Retrofl. Uteri	7.5	5
20	0	Retroflexio Uteri	8.5	..
20	0	Pelvic Inflammation	7	..
17	0	Dysmenorrhoea	6	..
26	0	"	9	3.5
53	9	Syphilis	7	5
31	1	Retrofl. Uteri. Relaxed Vag. Outlet	8	5
29	0	Pyosalpinx	8	4.5
63	8	Relaxed Vag. Outlet	7	6
56	6	" " " Hemorrhoids	7	5
37	4	" " " Retrofl. Uteri	7	6
35	1	Laceration of Cervix	7	2.5
28	6	" " " R. V. O. Retrofl. Uteri	8	6
34	3	Relaxed Vag. Outlet. Retrofl. Uteri	8	5.5
29	1	" " "	8	5
25	6	" " "	7.5	4
30	1	" " " Retrofl. Uteri	8	5
37	8	" " "	8	6
36	1	Myoma Uteri	7.75	8
40	4	Relaxed Vaginal Outlet. Retrofl. Uteri	8	8
23	1	Rupture of Recto-Vaginal Septum	6	4.5
24	2	Relaxed Vag. Outlet. Retrofl. Uteri	8	5
38	4	" " " Hemorrhoids	6	6
43	3	" " " Retrofl. Uteri	6	5
29	3	" " " " "	8	6
27	1	Myoma Uteri. Retained Secundines	6	5.5
18	0	Dysmenorrhoea	8	3.5
39	9	Relaxed Vag. Outlet. Retrofl. Uteri	5	8
52	10	Prolapsus Uteri	6	8
29	1	Relaxed Vag. Outlet	6.5	6.5
24	1	" " "	9.5	3.5
27	4	" " " Retrofl. Uteri	7	6
23	3	" " " Laceration of Cervix	12	6
38	2	" " " Retroversion of Uterus	7	6
39	4	" " "	6	5.5
52	0	Hemorrhoids	8	3
34	5	Relaxed Vag. Outlet	9	5.5
38	0	Dysmenorrhoea	8	3
20	0	Pelvic Inflammation	8	3
47	0	Appendicitis. Retrofl. Uteri	9	4.5
35	4	Relaxed Vag. Outlet	8	6
32	0	Dysmenorrhoea	6	..
32	1	Relaxed Vag. Outlet	9	6
34	5	" " " Retrofl. Uteri	9.5	5
41	6	" " " " "	8	6
29	3	" " "	6.5	5
23	0	Retroflexio Uteri	8	..
37	10	Double Vagina. Bicomued Uterus Relaxed Vag. Outlet	8	..
50	5	Relaxed Vag. Outlet. Retrofl. Uteri	6.5	7
36	3	" " "	10	5
32	3	" " " Retrofl. Uteri	7	9
26	1	" " "	7	7
26	2	" " " Pelvic Inflamm	8	6
28	2	" " " Hemorrhoids	7	5
37	7	" " "	8	9
23	2	" " "	7	8.5
30	2	Prolapsus Uteri	8	..
34	4	Relaxed Vag. Outlet. Retrofl. Uteri	8	6
22	2	" " "	8	6
25	2	" " " Retrofl. Uteri	8	6
35	1	" " "	8	6
28	2	" " "	6	6
39	3	" " "	6	5
42	1	" " " Retrofl. Uteri	12	7
33	3	" " "	8	7
26	1	" " " Hemorrhoids	10	5
26	2	" " " Retroversio Uteri	6	6

No. of cases, 100.
Average diameter of meatus in 100 cases, 7.59 mm.
Average diameter of meatus in nulliparous women, 7.83 mm.

ABSTRACT:¹ THE FREQUENCY OF GALL-STONES IN THE UNITED STATES.

BY CLELIA DUEL MOSHER, A. M., M. D.
(SERVICE OF DR. KELLY.)

Gynaecological Externe in the Johns Hopkins Hospital Dispensary.

(Read before the Johns Hopkins Hospital Medical Society, March 4, 1901.)

Although numerous statistics on the frequency of gall-stones have been published abroad, yet, as far as I know, there have not been given results based on a large number of cases in this country.

To determine the frequency of gall-stones in America, at Dr. Kelly's suggestion and with the permission of Dr. Welch, I examined the records of 1655 complete autopsies (Table I) from the Pathological Department of the Johns Hopkins Hospital. Of the 1655 records examined 1037 were males and 618 females; 634 were black and 1018 white; the color in the remaining 3 cases was not given. In 115 cases, or 6.94 per cent, gall-stones were present. All the percentages are larger than for my first 1000 cases, which were quoted by Dr. Kelly.² The reason for this has not been found. Roth at Basel published two sets of statistics (Diagram I) in which a similar difference is observed.

TABLE I.

Frequency of Gall-Stones in Persons of Different Ages in 1655 Autopsies, from the Pathological Department of the Johns Hopkins Hospital.

Age of patients.	Number of autopsies.	Number of cases with gall-stones.	Percentage of cases examined in which gall-stones were present.
0-20	232	1	0.43
21-30	277	5	1.80
31-40	333	18	5.40
41-50	328	29	8.84
51-60	258	34	13.14
61 and over	219	28	12.17
Age unknown	8
Totals.....	1655	115	6.94

The percentage of frequency of gall-stones in Germany, Austria, Switzerland and the United States is shown in Diagram I. It will be seen that the frequency in this country most nearly corresponds to that given by Rother for Munich.

Naunyn, in his treatise on cholelithiasis, bases most of his statements on the statistics of Schröder (Table II) who analyzed the cases from the Strassburg Hospital, where the autopsies include all periods of life. Prof. von Recklinghausen vouched for the fact that in no case had gall-stones been overlooked. The statistics for this country have been compared with those given by Schröder because of the great accuracy of the latter and the fact that the more complete data allowed exact comparison.

¹ This paper in full will appear in Vol. X of the Reports of the Johns Hopkins Hospital.

² Kelly, Dr. H. A.: A Rapid and Simple Operation for Gall-Stones found by exploring the Abdomen in the course of a Lower Abdominal Operation, in Med. News, Dec. 22, 1900.

DIAGRAM I.

The frequency of Gall-Stones in Germany, Austria and Switzerland as compared with the United States.

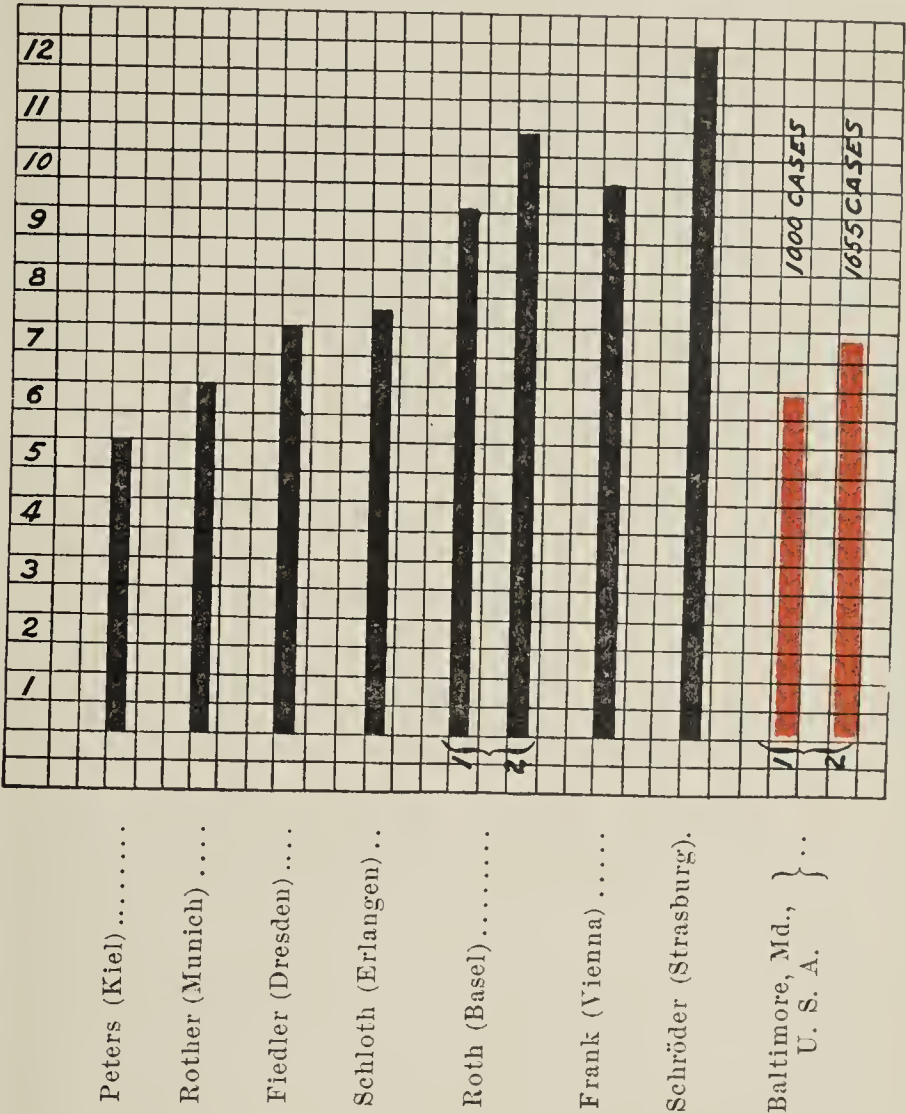


TABLE II.³

Frequency of Gall-Stones in Persons of Different Ages, according to Schröder.

Age of patients.	Number of post-mortems.	Number of cases with gall-stones.	Percentage of cases examined in which gall-stones were found.
0-20	82	2	2.4
21-30	188	6	3.2
31-40	209	24	11.5
41-50	252	28	11.1
51-60	161	16	9.9
60 and over	258	65	25.2
Totals.....	1150	141

Naunyn ascribes the variation in frequency of gall-stones in the statistics from different portions of Germany: (1) to the relatively larger or smaller number of young people included in any given number of cases; or, (2) to gall-stones being

³ Naunyn: A Treatise on Cholelithiasis; London, New Sydenham Society, 1896.

overlooked at autopsy. Although in the Johns Hopkins Hospital cases there is a somewhat larger proportion of young people included in the 1655 cases, a careful analysis shows that this fact fails to explain the much smaller frequency of gall-stones in this country. The second explanation is also inoperative here, as Dr. Welch has stated that gall-stones had not been overlooked in any case where they were present.

Age: Tables I and II show the distribution of the cases according to age groups.

Naunyn has called attention to the relative infrequency of gall-stones before the age of 30 years.

Diagram II shows the distribution according to age of both the German and American cases. The German cases are represented by the black line, the American cases by the red line. The irregularities in the German curve are probably apparent rather than real, the variation of the number of cases in each group probably being the reason. In Germany the greatest frequency appears to be after the 61st year, while in America the greatest frequency occurs between the 51st and 60th years. The American cases show a gradual

DIAGRAM II.

FREQUENCY OF GALL-STONES IN GERMANY AS COMPARED WITH THE UNITED STATES BY AGE GROUPS.

— Germany (Schröder), 1150 cases.
— United States, 1655 cases

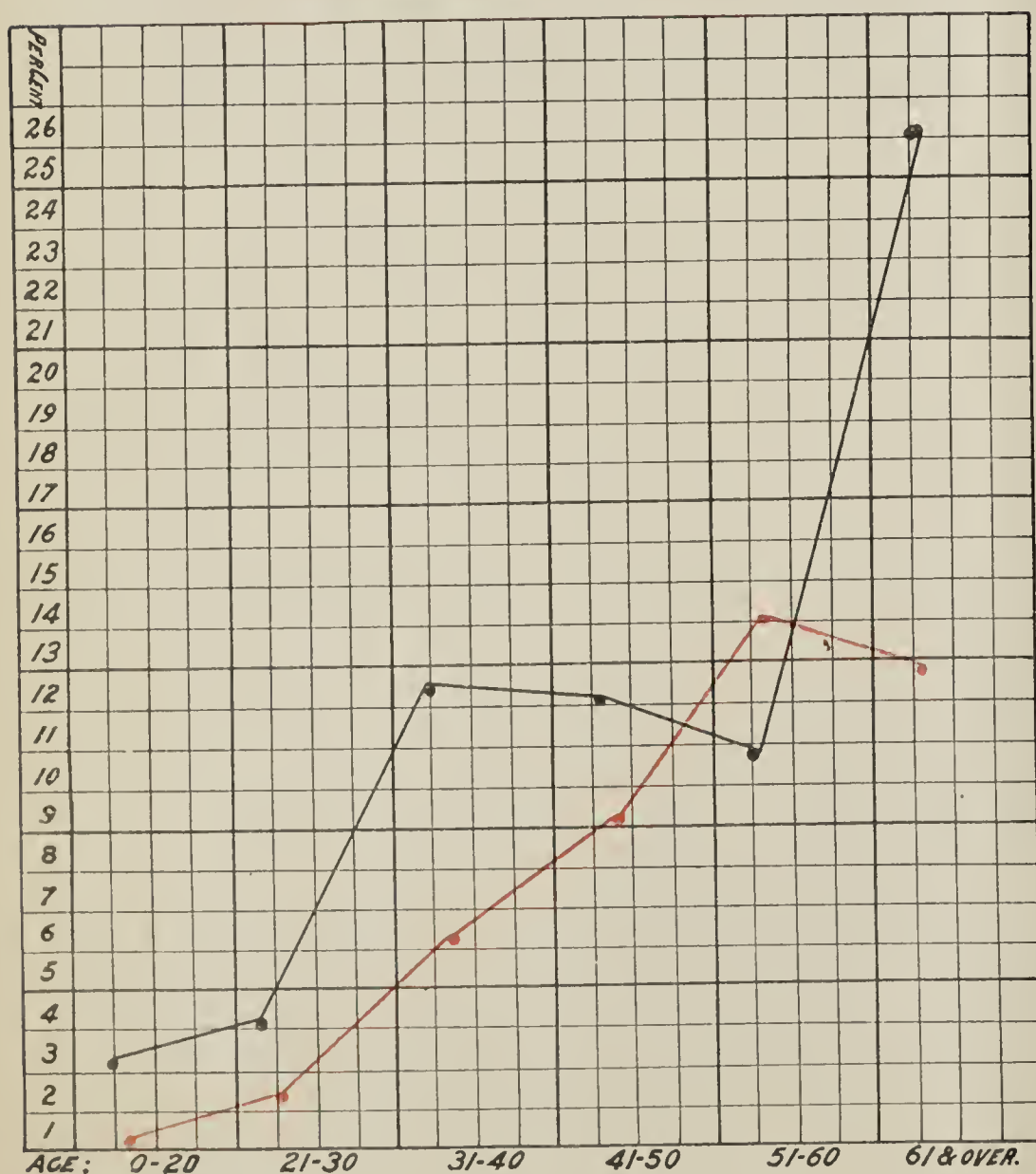
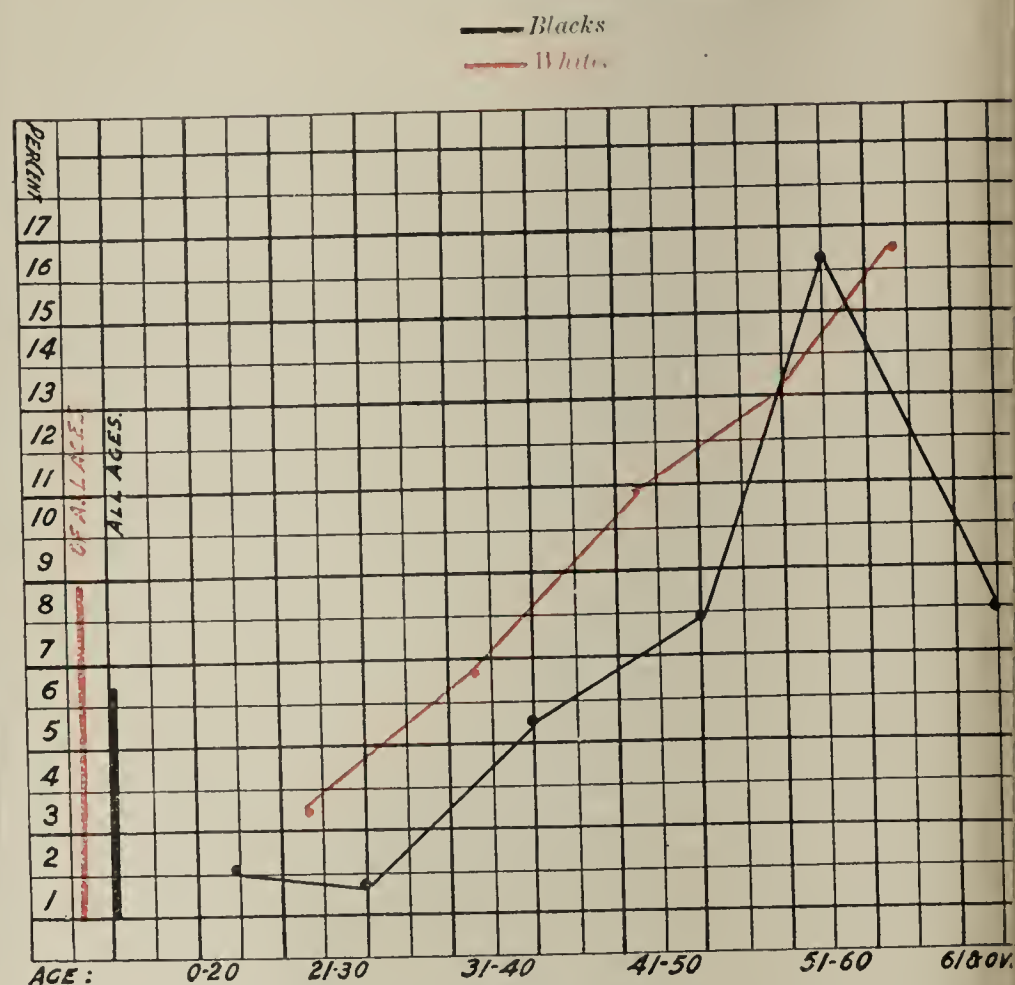


DIAGRAM III.

COMPARATIVE FREQUENCY OF GALL-STONES IN 1018 WHITES AND 634 BLACKS BY AGES (UNITED STATES).



and almost uniform increase in the percentage frequency to the sixtieth year. The slight falling off after this age is apparent rather than real, being probably due to the smaller number of cases included in this group. These cases tend to confirm the usual statement that gall-stones are rare before the thirtieth year and more frequent after that period.

TABLE III.

Frequency of Gall-Stones in Whites of Different Ages in 1018 Autopsies,
[From the Pathological Department of the Johns Hopkins Hospital].

Age of patients.	Number of autopsies.	Number of cases having gall-stones.	Percentage of cases examined in which gall-stones were present.
0-20	133
21-30	152	4	2.63
31-40	206	12	5.82
41-50	211	21	9.95
51-60	164	20	12.25
61 and over	145	23	15.86
Age not given	7
Totals	1018	80	7.85

TABLE IV.

Frequency of Gall-Stones in Blacks of Different Ages in 634 Autopsies,
[From the Pathological Department of the Johns Hopkins Hospital].

Age of patients.	Number of autopsies.	Number of cases having gall-stones.	Percentage of cases examined in which gall-stones were present.
0-20	99	1	1.01
21-30	125	1	0.8
31-40	126	6	4.76
41-50	115	8	6.91
51-60	93	14	15.05
61 and over	70	5	7.14
Age unknown	6
Totals	634	35	5.51

Race: Table III gives the cases of 1018 whites arranged in age groups, with number of cases having gall-stones and the percentage frequency in each group; Table IV gives the cases of 634 blacks, similarly arranged with corresponding data. Gall-stones occurred in 80 whites, or in 7.85 per cent of the cases, and in 35 cases, or 5.51 per cent, of the negroes. Pending a study of a larger series of cases, we must conclude that gall-stones occur somewhat less frequently in the black than in the white race.

Sex: Naunyn states that according to Schröder's statistics 20.6 per cent, or about one in every five women, have gall-stones. A striking difference is apparent in this country, for gall-stones were present in only 58 cases (9.37 per cent) of the 618 female bodies examined. Therefore, in this country only one woman in every 10 or 11 would appear to have gall-stones—a frequency less than half as great among American as compared with German women.

DIAGRAM IV.
COMPARATIVE FREQUENCY OF GALL-STONES IN MALES AND FEMALES
BY PER CENT OF ALL AGES COMBINED (United States).

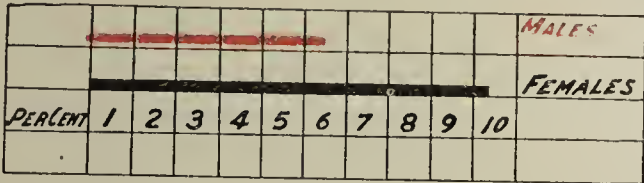


DIAGRAM V.
COMPARATIVE FREQUENCY OF GALL-STONES IN MALES AND FEMALES,
BY PER CENT OF ALL AGES COMBINED (Germany).

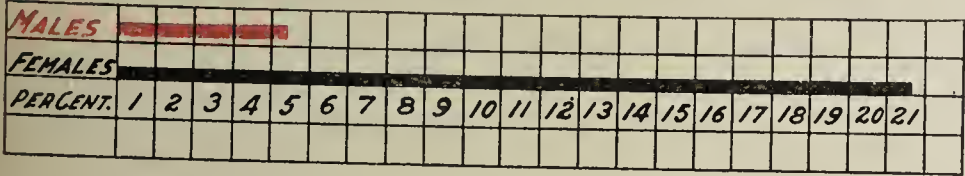


Diagram IV gives the comparative frequency of gall-stones in males and females in the United States, based on Johns Hopkins autopsies. The difference in frequency as compared with Germany is seen by comparing this with Diagram V, which is based on Schröder's cases, as quoted by Naunyn.

TABLE VI.
Frequency of Gall-Stones in Males of Different Ages in 1037 Autopsies,
[From the Pathological Department of the Johns Hopkins Hospital].

Age of patients.	Number of autopsies.	Number of cases having gall-stones.	Percentage of cases examined in which gall-stones were present.
0-20	107
21-30	180	3	1.11
31-40	202	7	3.46
41-50	213	13	6.10
51-60	170	14	8.23
61 and over	162	20	12.28
Age unknown	3
Totals.....	1037	57	5.49

TABLE VII.
Frequency of Gall-Stones in Females of Different Ages in 618 Autopsies,
[From the Pathological Department of the Johns Hopkins Hospital.]

Age of patients.	Number of autopsies.	Number of cases having gall-stones.	Percentage of cases examined in which gall-stones were present.
0-20	125	1	0.8
21-30	97	2	2.06
31-40	131	11	8.39
41-50	115	16	14.00
51-60	88	20	22.70
61 and over	57	8	14.21
Age unknown	5
Totals.....	618	58	9.37

Apparently the men in the United States have gall-stones in 5.49 per cent of cases as compared with 4.4 per cent for the German men, or about one per cent more frequently. Tables VI and VII give respectively the number of cases of males and females in the Johns Hopkins autopsies, arranged according to age groups, the number of cases occurring in each group, and the frequency of gall-stones for each age in percentage.

DIAGRAM VI.
COMPARATIVE FREQUENCY OF GALL-STONES IN 1037 MALES AND 618
FEMALES BY AGES (UNITED STATES).

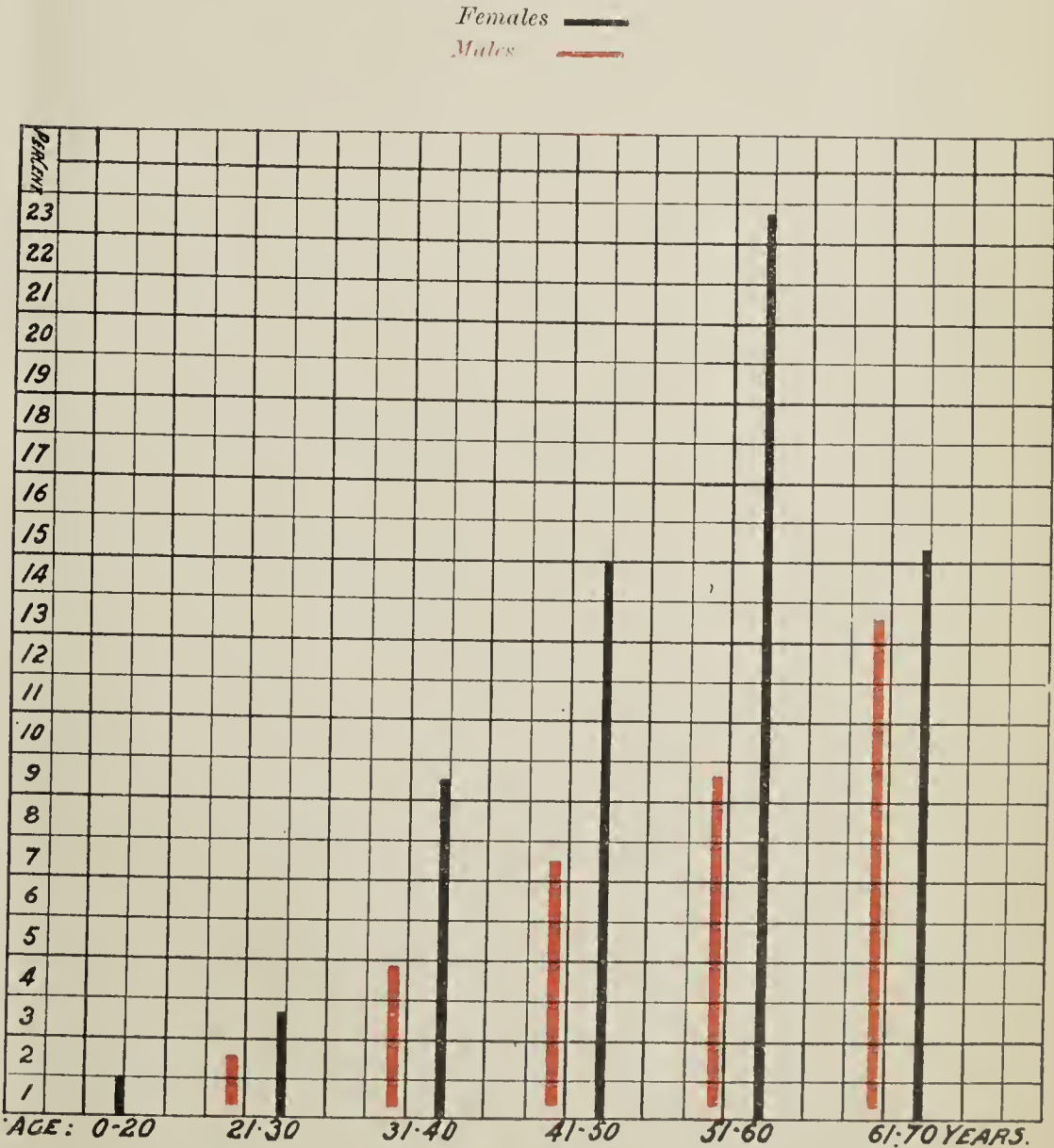


Diagram VI graphically shows these results. The black lines represent the frequency for the females in percentage in each age group, the red lines the frequency for the males. Again the females in the group of from 51 to 60 years old reach the maximum frequency of cases having gall-stones, and there is a falling off in the succeeding group of 61 years and over. If we refer to Table VII, it will be seen that the number of cases in the last group is rather smaller than in the preceding one, while a slighter difference in numbers is seen in the corresponding group of males. If we compare the character of the curve for the blacks in Diagram III, where the whole number of black cases was 634 as compared with the 1018 white cases, and remember that there are only 618 females as compared with the 1037 males, it will be seen that the two curves based on the two larger groups of cases correspond very closely in character, showing an almost uniform increase from age group to age group, both reaching their maximum in the last group. Of the two curves based on the smaller number of cases, 634 in one, and 618 in the other, both show the maximum frequency in the age group of 51 to 60 years. I am at a loss to explain this fact unless it be due to the smaller number of cases included in this last group.

Etiology: Naunyn has ascribed the greater frequency of gall-stones in women to wearing of tight clothing and to pregnancy, each of which hinders the flow of the bile. Schröder found gall-stones in more than half of the cases having a tight-lace furrow on the liver. Reidel showed that the deformity of the liver from this cause disturbed the normal situation of the liver, especially affecting the gall-bladder, which is turned downward, the cystic duct being stretched and the emptying of the gall-bladder made more difficult. Among the Johns Hopkins cases there was but one (Path. No. 988) in which this was noted. In this the gall-bladder had to be placed in a certain position before the fluid bile could be squeezed through the patent ducts, because there was a sharp deflection in the cystic duct. Wiesker demonstrated that the ligamentum hepato-duodenale is stretched in cases of floating liver or of floating right kidney; this also affects the cystic duct and hinders the emptying of the gall-bladder. Litten also pointed out that movable kidneys may cause biliary obstruction. Mignot, Gilbert, Fournier, Cushing and others have produced gall-stones experimentally in animals by the inoculation of attenuated cultures of the bacillus coli communis or bacillus typhosus. Dr. Cushing⁴ calls attention to the necessity of producing the necessary catarrhal inflammation of the gall-bladder before calculi will form even when the organisms are present. Naunyn has also stated the two factors necessary to the formation of gall-stones to be stasis of the bile and the presence of organisms. Dr. Welch has also shown by the culture of streptococci as well as bacillus coli communis and bacillus typhosus that more

forms than the two latter organisms may be concerned in the formation of gall-stones in the human subject.

Attention has been called to a number of the several favoring conditions which may produce stasis of bile in women. It may be worth while to enumerate them briefly once more.

1. Clothing: (a) changing diaphragmatic to the costal type of respiration and thus the absence of diaphragmatic action producing a stasis of the bile; for, according to the statements of Naunyn, Heidenhain and his pupils have proved experimentally that the descent of the diaphragm is an important factor in emptying the gall-bladder; (b) or causing gross lesions, such as the tight-lace furrow or long liver lappets, leading to displacements which cause mechanical obstruction to the outflow of the bile.

2. Lax abdominal walls, whether from inactivity or too frequently repeated pregnancies, and enteroptosis, by which the emptying of the gall-bladder may be hindered through the alteration of the relations of the gall-bladder and its ducts.

3. The presence of large abdominal or pelvic tumors, such as a large myomatous uterus or even in some cases the gravid uterus, thus producing pressure which may cause stagnation of the intestinal contents—a favorable condition for the invasion of the bile passages by the ever-present colon bacillus.

4. The great frequency of puerperal infections of varying intensity, as well as the numerous cases of pelvic inflammatory disease of other origin, with peritonitis and adhesions, may certainly furnish a number of cases of mechanical obstruction as well as sources of infection. In the male sex there is no corresponding group of possible sources of mechanical obstruction to outflow of the bile which can be compared with these favoring conditions in the female to the formation of gall-stones. It would seem probable that any one of these factors, acting singly, would be sufficient to explain the greater frequency of gall-stones in women.

Some authors have called attention to the frequency of gall-stones in the poor and badly nourished, while others have held that gall-stones occur more frequently in the rich and overfed classes. In order to determine this question, the cases from the Bay View Asylum and Almshouse service have been separated from the whole body of cases. By the courtesy of Dr. Opie of the Pathological Department, it was possible to get the records of 125 cases from the Bay

TABLE VIII.
Frequency of Gall-Stones in Persons of Different Ages, in 125 Autopsies,
[From the Pathological Service of the Bay View Asylum and Almshouse.]

Age of patients.	Number of autopsies.	Number of cases having gall-stones.	Percentage of cases examined in which gall-stones were present.
0-20	6
21-30	13	1	7.69
31-40	16	2	12.05
41-50	20	2	10.
51-60	20	3	15.
61 years and over .	50	8	16.
Totals.....	125	16	12.8

⁴ Cushing, Harvey: Observations upon the Origin of Gall-Bladder Infections and upon the Experimental Formation of Gall-Stones, in Johns Hopkins Bulletin, Vol. IX, pp. 166-170.

View service. Table VIII gives these cases arranged in age groups, which makes it possible to contrast these cases with exactness.

Of the 125 cases from the Almshouse and Asylum 16, or 12.8 per cent, had gall-stones, as compared with the frequency of 6.94 per cent for all cases considered together. In other words, gall-stones were present in the Bay View cases almost twice as frequently as in the 1655 autopsies.

This increased frequency in the Bay View cases is partially but not wholly explained by the greater number of cases over 30 years of age in Almshouse and Asylum autopsies. The numbers are too small to warrant any conclusions at this time.

In 115 cases of the 1655 autopsies gall-stones were present. Death was to be attributed to their presence or effect in only 13 cases; in the remaining 102 cases the gall-stones were merely incidental.

The number of stones present, when specified, varied from 1 to 250 stones. The location of the calculi was as follows:

In gall-bladder alone.....	in 86 cases.
“ and common duct.....	6 “
“ and cystic duct.....	10 “
“ and hepatic duct.....	1 “
In gall-bladder and common and cystic ducts.....	2 “
“ “ common and hepatic ducts.....	1 “
“ “ common, cystic and hepatic ducts.....	2 “
“ “ common, cystic, hepatic and the larger ducts of the liver.....	1 “
“ “ common, hepatic and larger ducts of the liver.....	1 “
“ “ larger ducts of the liver.....	1 “
In common duct alone.....	1 “
In cystic duct alone.....	1 “
Common and hepatic ducts.....	1 “
Location not specified. (Stones removed at previous operation.).....	1 “
115 cases.	

From this classification it will be noted that gall-stones were present in the gall-bladder in 111 cases. In only 4 cases was the gall-bladder free from concretions when their presence was noted in any other portion of the biliary system. Biliary calculi were found in the ductus communis choledochus in 15 cases; in the cystic duct fifteen times; in the hepatic duct seven times, but always in association with calculi in other portions of the biliary system. Biliary calculi were found in the ducts of the liver in two cases. In the first case (Path. No. 1402) the concretions were only in the larger ducts of the liver; but in Path. No. 1530 the calculi were present in both the larger and smaller ducts. In 6 cases concretions were present at the papilla or the Diverticulum of Vater.

The condition of the biliary system was as follows:

Gall-bladder condition was noted in 28 cases. The gall-bladder was distended in 22 cases, not distended in 1, and reduced in 5 cases. There were adhesions about the gall-

bladder in 14 cases; the peritoneum over the gall-bladder was thickened in 9 cases. The mucous membrane was thickened in 10 cases, eroded in 1, and necrotic in 2 cases. One case showed healed scars, and in 4 cases the mucous membrane was infected; in 4 cases the mucous membrane was stated to be normal.

Cirrhosis of the liver was present in 21 cases. There were liver adhesions in 24 cases. The capsule was thickened in 11 cases. Several small phleboliths were present in one case. The tight-lace furrow was noted in 4 cases, three times in women and once in a man.⁵ A long liver lappet was present in 6 cases.

If we consider the gall-bladder adhesions and the adhesions about the liver, the number of cases in which mechanical obstruction to the flow of bile was possible is fairly frequent.

The condition of the bile was as follows: In 33 cases it was described as viscid, thick or tenacious, and in 1 case inspissated; in 10 it was cloudy or turbid; in 3 cases there was a granular sediment and in 1 case the bile contained solid particles. In one case the bile was so tenacious that it could not be squeezed through the patent ducts. In 11 cases it was described as fluid or thin. In 3 cases there was a mucous plug in the mouth of the common duct which had to be expressed before bile could be squeezed into the intestine. The above conditions might be grouped under a general head—cases in which was present mechanical obstruction, which might interfere with a flow of the bile. (1) Adhesions about gall-bladder or liver; (2) interference with the free movements of the diaphragm in respiration, indicated by the presence of tight-lace furrow on the liver; (3) changes in the bile itself when its fluidity is lost; (4) mucous plug in mouth of common duct.

Infections: Twenty-four cases were recorded in which was made a bacteriological examination of the bile. In 11 cases the bile was sterile. *Bacillus coli communis* was found in 7 cases; *B. proteus vulgaris* once; *B. coli communis* with the *Diplococcus lanceolatus* twice; the streptococcus was found in one case. Bacteriological examination of the gall-stones showed them negative in three cases. *B. coli communis* was present in one case, and a capsulated bacillus in another. Dr. Welch states that in addition to frequently having cultivated *B. coli communis* from gall-stones⁶ he has also cultivated *B. typhosus* and the streptococcus.

In the cases where the bile and gall-stones are recorded as sterile, I understand it to mean that they were sterile as far as the ordinary pyogenic organisms are concerned, no special cultures being made to show the possible presence of the tubercle bacilli or the gonococcus.

In 12 cases there was recorded a previous history of typhoid fever. In 6 cases no bacteriological examination of

⁵ Welch, William H.: The Bacteriology of Surgical Infections, in Dennis' *System of Surgery*, Vol. I, p. 265.

⁶ Fitz, G. W.: A Study of Types Respiratory Movements, *Journal of Exp. Med.* Vol. I, p. 678.

stones or bile was made. In one case the bile and stones were sterile, and in one the stones were sterile. *B. coli communis* was present in the bile once; *B. subtilis* was found in the bile once; and the streptococcus was present once. In none of the 12 cases was *B. typhosus* recorded as being present.

The pathological conditions found were as follows:

Tuberculosis was noted in 14 cases, or 12.17 per cent.

Arterio-Sclerosis: Benecke has called attention to the great frequency of atheromatous degeneration with gall-stones. According to Naunyn the statistics of Sloth (Erlangen) and Schröder (Strasburg) have not strongly supported Benecke's statements. They found atheroma in about 25 per cent of their cases. Here there was arterio-sclerosis in 50 cases, or in 43.48 per cent of the 115 cases in which gall-stones were present.

Nephritis was the most frequent of all the associated conditions found. In 69 cases there was definite nephritis and in 9 additional cases there were lesions of the kidneys sufficient to interfere more or less with proper functioning, making a percentage of 72.17.

Uterine myomata were present in 13, or 22.43 per cent, of the 58 cases in which gall-stones were found in women. In 48 women whose gall-bladders Dr. Kelly explored in the course of a lower abdominal operation, gall-stones were found in 7 cases, or 14.5 per cent.⁷ On examining the list it is found that every case, or 100 per cent, of these cases in which Dr. Kelly had found gall-stones had been operated upon for either myoma or large ovarian cyst. While the number of cases is too small to form any definite conclusions, this fact suggests a possible association due to pressure.

Carcinoma of gall-bladder occurred in 2 cases. Lumbroicoid worms were found in the gall-bladder in 2 cases. Pancreatitis was present in one case (Path. No. 1574). Pancreatitis with fat necrosis⁸ was noted in four cases (Path. Nos. 211, 1530, 1567, 1614).

In 22 cases in which no definite concretions existed, there were abnormal conditions of the bile which suggested the possibility of a preliminary stage to the formation of gall-stones. The bile was described as follows: bile contains granular sediment; sandy particles; friable dark sediment, soft brown irregular flakes; flocculi, which on examination prove to be clumped typhoid bacilli; small masses of blackest pigment, etc.

Among our 115 cases, floating kidney was noted but once. In the Johns Hopkins cases, tight-lace furrow was recorded but four times, three times in women and once in a man as has been stated. Fitz has called attention to the effect on respiration of the wearing of tight belts by men. It is conceivable that since the type of respiration in women may be modified by tight lacing and a similar change produced in men by the wearing of tight belts, a deformity of

the liver produced by tight lacing in women might also be produced by the wearing of a tight belt by a man. Among the 58 women having gall-stones, only 3, or 5.17 per cent, had the tight-lace furrow; if we include those cases having a long liver lappet as possibly due to constriction, it amounts to only about 19 per cent in which these lesions could possibly be considered an etiological factor.

Naunyn also states that, apart from these gross lesions, the bile stream is liable to be hindered by the dress of women and in pregnancy. He quotes Heidenhain and his pupils as having proved by experiment that the expulsion of the bile from the common duct is materially aided by the movements of the diaphragm.

My own experimental work on respiration has demonstrated that pregnancy interferes less with the respiration than has generally been believed. The respiratory movements in the different regions tend to become equalized, but the diaphragmatic respiration persists as late as the eighth and even the beginning of the ninth month of pregnancy. My experiments clearly demonstrate that clothing is the most potent factor in the production of costal type of respiration in many women.

It has been seen that myomata have been found in 22.43 per cent of the 58 women having gall-stones, and Dr. Kelly in operative cases has found gall-stones in 14.5 per cent of the cases where the gall-bladder was explored in the course of a lower abdominal operation; 100 per cent of his cases in which the gall-stones were present were operated on for myoma or large ovarian cyst. If the gravid uterus is an etiological factor in the formation of gall-stones, should we not rather look to the pressure effects as shown by any pelvic or abdominal tumor, as favoring such formation by producing constipation, than to the action on the diaphragm as the mode of action?

Conclusions: Pending the study of other series of cases from various parts of the United States, we may draw the following conclusions:

Nationality: On the basis on the analysis of the 1655 autopsies from the Johns Hopkins Pathological Department, as compared with 1150 (?) cases as given by Schröder of Strassburg, gall-stones are less frequent in the United States than in Germany, the United States showing a frequency of 6.94 per cent, Germany of 12 per cent.

Age: The frequency of gall-stones in a given number of cases will increase with the age of the patients examined. The American cases tend to confirm the statements of previous observers that gall-stones are rare before the thirtieth year and more frequent after that age.

Color: Gall-stones are more frequent in the white than in the black race, the American cases showing a frequency of 7.85 per cent in the whites and 5.51 per cent in the negro.

Sex: Women are more liable to have gall-stones than are men, the American cases showing the frequency in 618 women to be 9.37 per cent, and in 1037 men to be 5.94 per cent. The American women have gall-stones only about half as frequently as the German women. In the United

⁷ By an error the percentage frequency of gall-stones was printed in Dr. Kelly's article as 8 per cent when it should have read 8 cases.

⁸ Opie, Eugene L.: The relation of Cholelithiasis to Disease of the Pancreas and to Fat Necrosis, in Amer. Jour. of Med. Sci., Jan. 1901.

States only about one woman in every 10 has biliary calculi, while in Germany, according to Naunyn, gall-stones are found in 20.6 per cent, or in about one woman in every 5.

DISCUSSION.

Dr. Kelly: I am sure all have listened with much satisfaction to this well prepared and interesting paper by Dr. Mosher. It is particularly satisfactory to me that we send out from this Society the first elaborate statistics compiled on this subject in America. The immediate occasion of Dr. Mosher's investigation was that I have recently, whenever

making a large enough abdominal incision, made an exploration of all the abdominal organs, and in these cases I have found about 14.5 per cent of gall-stones with more or less extensive pathological changes. In each instance I removed the stones by a simple and rapid operation by pushing the stone up against the abdominal wall from within, while cutting down from the outside on the hard body; I then everted the gall-bladder, incised it, and the stones were popped out. It then became a matter of interest to know just how frequently gall-stones were found, and Dr. Mosher has taken up the work and has made a wide and thorough investigation.

TENDON TRANSPLANTATION.¹

BY SYDNEY M. CONE, M.D.

Fertile fields in physiology have been opened up before now through work done in the pathological laboratory. How much did the degeneration of nerve tracts aid in working out the anatomy of the cord?

There is no present knowledge of the limit to which the questions brought up and answered in the recent work on tendon transplantation will lead. Some very interesting physiological as well as surgical facts are before us.

Nicoladoni, in 1881, successfully changed the position of some active tendons in a paralytic club-foot to take the place of the paralyzed muscles. In the three cases reported he improved the mechanism of the feet very greatly. It seems that the operation should at once have taken a firm position in surgery.

It was not until Goldthwait published his cases in 1896 that the subject was again brought before us. Since then in Germany, France and the United States a number of orthopedic surgeons have demonstrated the great value of tendon transference. Its position in surgery is assured, not only because of the great usefulness of the procedure, but also because of the absolute safety and exact surgery of the operation. It is used in various conditions. Goldthwait, Bradford, Vulpius and Hoffa have described fully the method of application for deformed feet following infantile paralysis. Eulenberg, Hoffa and Vulpius wrote of its application to the cure of the spastic condition in Little's disease. Rochet, Townsend, Franke, Drobnik, Vulpius and others described the use of tendon anastomosis in musculo-spiral paralysis. Goldthwait, Vulpius and Milliken carried the active sartorius over into the fascia of the quadriceps femoris. Hoffa united the deltoid to the paralyzed triceps.

Vulpius and Hoffa both claim the usefulness of this operation in cases of muscular dystrophy. Eulenberg and Hoffa suggest the advisability of using implantation in case of apoplexy paralysis. It has been used successfully after traumatic paralysis or where muscles were congenitally absent.

Kunik, in naming the operations according to how the tendons are united gives four forms. He adds to the "active," "passive" and "active-passive" forms of Hoffa a method used by Goldthwait—transplanting the periosteal insertion of the tendon to another place on the bone. Goldthwait used this in relaxation of the patellar ligament with dislocation of the bone. As a rule, Lange, of Munich, uses the periosteal method. He adds to the technique an original and interesting method of lengthening the tendons which he desires to transplant. If in carrying the biceps and semitendinosus around the femur to take the place of the quadriceps, he finds these united tendons too short, he supplies the deficiency with silk, which he sews to the periosteum at the tubercle of the tibia. Not only do these two posterior muscles take the place of the anterior paralyzed one, but the tissue thickens about the silk and makes a permanent attachment. The other three methods are named differently by various operators.

Hoffa refers to the union of a divided sound tendon into a paralyzed one as "active"; Vulpius calls this a "descending" transplantation, while Kunik uses the expression "intraparalytic implantation." When the divided distal end of a paralyzed tendon is carried to the sound, undivided tendon, Hoffa uses the term "passive," Vulpius names this "ascending" transplantation, while Kunik calls it "intrafunctional implantation." Where both are divided and united both names are combined, a hyphen separating them, *e.g.* "active-passive."

Having determined that the operation is necessary, the method to pursue is, as a rule, determined simply by the anatomy of the part involved. Hoffa gives a schedule of various paralyses, their accompanying deformities, and suggests the method of transplantation suitable for the case in hand.

It is conceivable in some instances that owing to changed anatomical conditions, other methods of effectual tendon transference might be adopted. Goldthwait demonstrates this in the pictures he shows of the unusual action of the

¹ Read before the one hundred and third Annual Meeting of the Maryland Medical and Chirurgical Faculty, April 25, 1901.

peronei muscles when, after long paralysis of the posterior group of leg muscles, they are carried forward in front of the malleolus. Again, in case of the sartorius, the action differs according to the amount of padding forming the fulcrum for it to act upon. It is not difficult to abstract the best from what has been written on this subject up to the present time.

Before deciding to operate, the patient must have had every possible chance for the relief of the deformity. Massage, electricity, active and passive movements are usually recommended for one or two years before advising operative measures. If immobility prevents the limb being placed in a good position, "redressement" must precede the operation.

A thorough electrical and physical examination must be made. One cannot always depend upon the intelligence of the patient in determining what muscles are intact. It may even be necessary to await the first incision before we learn the condition of the muscles. The normal muscle is dark red, the parietic muscle is rose red, while the completely paralyzed muscle is yellow. While the method of uniting the tendons differs, it is generally conceded that the least possible traumatism to sheath and tendon is required. The broadest union one can get and a freshly serrated surface are desirable. Silk is generally conceded to be the best suture material. Quilted sutures are preferred as a rule.

The first dressing is done in nine days, but the limb must remain in plaster for about five weeks, after which massage and passive action may be adopted.

It is usually noted that the new arrangement works well at the first dressing.

There are few variations in the method of treating the same paralytic condition. In musculo-spiral paralyses, Rochet, Franke, Vulpinus, Drobnik and Townsend have had the greatest experience. They agree that it is usually necessary to shorten one or more of the extensor tendons, transplanting a flexor muscle at the same time. The flexor muscle most commonly recommended to be used is the flexor carpi ulnaris. Townsend advises carrying it between the radius and ulna, while other operators prefer to wind it around the wrist. The operations upon the foot present few alternatives as seen from Hoffa's schema.

When the newly transplanted muscle takes on its new work shortly after the tenth day one is led to question how this is to be explained. How is it that a flexor extends? How explain that a muscle accustomed to act through being stimulated by a nerve looked upon as governing one kind of motion, now changes its way of acting under the same nerve influence? It would seem that the changed condition of things in the periphery causes a changed central (brain) arrangement. The nerves have no specific action, they are merely the connecting links between muscle and brain.

Lange made a most interesting observation in cases IV and V of his series, where he split the tibialis anticus tendon and attached one portion to the cuboid bone. This muscle learned to perform two separate movements—inward and outward rotation of the foot. If one and the same muscle

can be thus doubly educated, it should not seem strange that when relieved of all its original duties it could accommodate itself to a new simple brain-muscle relationship.

It is due to a rapid re-education of the transplanted muscle, which is more apt to take place in youth "before the frequently practiced coordinated actions, especially those associated with position, have become fixedly automatic" (Eulenberg).

Drobnik says that the nerve centres accommodate themselves properly within certain bounds to the changed grouping of the muscles.

Eulenberg says "It is not only possible, but in the highest degree probable, that excitations are set up in a centripetal manner in the cortical portion of the brain which regulates coordination. These can connect themselves with regulating impulses starting in the cortex, which impulses were meant for other work and purposes. These central apparatuses, commanding and regulating the coordinating mechanism, must possess a much greater adaptability in young children than in adults, in whom the more important and oft-exercised coordinated actions, especially those associated with place, have become fixed in firmly arranged automatic actions. The artificial peripheral switching off of the centrifugal innervation into other antagonistic muscles for purposes of divided function or transferred function must cause changes in the centripetal impressions and reactions. Probably this change will shut off tracks already present and form new routes. Thus we would get a new regulation of the whole innervation founded on the new functional needs."

This will explain any of the problems in this much-discussed field. It even touches the question one must ask when, in a case like the one I shall describe, following correction of the deformity of the foot the paralyzed thigh muscles recovered their activity. It would seem that having a group of muscles which have been educated together, several of them being lost, the rest do not get the centrifugal stimuli they formerly got because the centripetal stimuli were wanting. Now, when the old centres in the brain are again stirred up by centripetal stimuli, after the operation on a few of the paralyzed muscles which were accustomed to start the motion in the coordinated movement, all get the centrifugal stimulus thus set up.

The case to be reported is that of a girl (K. S.), 7 years old, admitted to the Robert Garrett Hospital, Jan. 9, 1901.

She had been lame for four years, dragging the left limb in an everted position. The foot was in the position *cavus* and had little support at the ankle joint. It was slightly pronated. Very little information could be obtained from the mother about the origin of the paralysis. It came on suddenly while the child was in good health. The child began to limp, the leg wasted, and the skin took on the appearance of "goose skin."

Examination showed the left limb to be from 2-5 cm. smaller than the right one. Electrical and physical examination showed paralysis of the tibialis anticus, gastrocnemius, soleus, tibialis posticus and flexor longus pollicis. She could

not invert the limb at all, whether from paralysis of the semimembranosis and tendinosis gluteus medius or tensor vagina femoris, or to all, I could not determine. No electrical response was noted in any of these muscles.

On Jan. 22, under ether, an incision was made 8 cm. long across the tendo Achilles. The peroneus longus and brevis were exposed and cut across near their insertions. The peroneus brevis was carried under the tendo Achilles and through an opening in the flexor longus pollicis. The peroneus longus was serrated and passed through a slit in the width of the tendo Achilles. Quilted sutures were used to fix them as described by Goldthwait. A silver wire subcutaneous suture closed the wound. In ten days (Feb. 1) the first dressing was made, showing union *per primam*. The child was kept in plaster for three weeks, then given massage and passive movements. She soon began to walk without a plaster dressing. It was noted at once that she turned the foot in, although there remained a tendency to outward rotation when she did not try to hold her limb in the correct position. To correct the supination and laxity of the support on the inside of the foot, I did the second operation on April 5. The opportunity to do these operations was afforded me through the kindness of Dr. Platt.

An incision 6 cm. long was made above the annular ligament, exposing the tibialis anticus and extensor longus digitorum. A section of the tibialis was carried through an opening made in the extensor longus digitorum and held there with quilted sutures.

The skin suture was silver wire. The first dressing was done in eight days. The wound had healed *per primam*, and the contraction of the extensor longus digitorum drew the foot in and up. The patient left the hospital in four weeks with the foot in plaster. The child is now at home, being treated with massage, passive and active exercise. She has perfect plantar flexion and improved use of her dorsal foot muscles, and will doubtless continue to increase the activity of her newly acquired movements.

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PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

February 18, 1901.

In the absence of the president, the meeting was called to order by Dr. Osler.

Chorea with Embolism of Central Retinal Artery. DR. THOMAS. **Ophthalmoscopic Appearances.** DR. REIK.

(To appear in a future number.)

Volvulus of Meckel's Diverticulum with Recovery after Operation. DR. WILLIAM J. TAYLOR, of Philadelphia.

(To appear in October BULLETIN.)

Monday, March 4, 1901.

In the absence of the president, the meeting was called to order by Dr. Kelly.

Exhibition of Medical Cases. DR. McCRAE.

The cases I will show this evening are cases of severe anæmia that might well be called pernicious anæmia. They

are now to be shown, however, on account of some associated symptoms.

The younger is aged 38 and came in complaining of stiffness in the arms and legs with some numbness. His present illness dates back to the summer of 1898, when he was somewhat "run down." He continued to work until March, 1900, when he was compelled to stop on account of shortness of breath and weakness. In the January previous he had a carbuncle of the neck which presented nine openings. He has a curious waxy, yellow color, is very weak and has sometimes shortness of breath.

I would like first to call attention to a symptom that may have some bearing on the cause of pernicious anæmia. You are probably all familiar with the recent writings of Dr. William Hunter, who has suggested that pernicious anæmia is often due to foci of suppuration, sometimes even so simple as a carious tooth. On examination we found this patient's teeth exceedingly bad, and he tells me that has been his condition for five years past.

His blood shows no special features beyond a hæmoglobin estimate of 50%, a red count of 2,500,000, and leucocytes 2000, with 45% of mononuclears and an occasional nucleated red cell. Coming to the sensory symptoms of which he complains, namely, numbness and tingling, we have not made out anything peculiar on examination about sensation which appears to be normal. His knee-jerks are exaggerated.

The other case, a patient of 58, has been in the hospital since the 8th of October. He complained of numbness of the limbs and pain along the spine, his symptoms dating back for a period of 18 months. His first symptom was weakness. He fell down stairs one day and after that was unable to work for some time. His blood on admission showed 1,900,000 red cells, a hæmoglobin of 48%, and 48% of mononuclears. On admission he showed a curious tottering gait and was almost unable to walk unsupported. He had no Romberg sign and the knee-jerks were somewhat exaggerated. He has improved very much, but still walks with some hesitation and holds himself stiffly. The knee-jerk has gradually diminished until now it is only elicited with some difficulty. His hæmoglobin went up to 70% and the red corpuscles to 3,500,000 per cmm.

The whole group of spinal symptoms in connection with anæmia is extremely interesting, although as yet the subject is in a rather chaotic state. One can separate undoubtedly a group of cases of which this man is a type that are associated without doubt with pernicious anæmia. A number of cases have been reported from the National Hospital for Nervous Diseases in London that occurred after anæmias that are evidently secondary anæmias.

In anæmias, three types have been described: one where the anæmia is primary, a second where the cord changes are primary and anæmia develops later, and a third where with anæmia there are no symptoms of spinal cord involvement during life, but it is found on section. The coincidence of these two cases is interesting.

In regard to the question of treatment, I think this young

man should undoubtedly have his mouth carefully attended to, the carious teeth drawn and the mouth cavity cleaned up as well as possible. In addition to that, he is getting arsenic and good feeding. The outlook is difficult to determine. In the other case, judging from the cases reported, the progress is probably downwards. Three stages of that have been described: First, a spastic condition; second, the condition in which he is now; and thirdly, a perfectly flaccid paralysis that usually ends fatally. He has been having the ordinary treatment of good food, arsenic and fresh air. In the last two or three weeks he has lost nearly a million red blood-corpuscles, but there is no increase in the spinal-cord symptoms in connection with that drop.

DISCUSSION.

DR. THAYER.—Within the last two years I have seen two very interesting cases of pernicious anæmia with symptoms of involvement of the cord. In the first instance, seen last year with Dr. Watson, the patient developed a very high degree of ataxia of both lower and upper extremities and loss of reflexes. There was incontinence of urine and feces.

The second case I saw about two weeks ago with Dr. Beck. The first symptoms of her anæmia began during the heated term last summer. During the fall she began to have difficulty in using her fingers and her hands became weak. There was considerable numbness and tingling. She was unable to button her clothes. Shortly afterwards she began to have the same sensations in her feet and noticed a certain unsteadiness of gait. On several occasions she fell. When seen the patient showed a high degree of anæmia, only about 1,500,000 red corpuscles; there was no marked atrophy in the upper extremities, but great weakness of the muscles in the arms and hands. A distinct increase of the reflexes at the elbows and wrists. There was fairly well-marked ataxia, especially of the right hand, the patient being unable to unbutton her clothes. There was no atrophy in the legs or thighs, no fibrillary tremor; knee-jerks diminished but still present. On superficial examination sensation to touch and pain was normal throughout. The patient distinguished the head and point of a pin well in both arms and legs.

With regard to the question of treatment of pernicious anæmia, it is interesting to note that Dr. Cabot, who has seen a large number of cases, is of the impression that arsenic is of little or no value. He states that rest, fresh air and judicious feeding are the most important points in treatment. I must say that this statement has seemed to me rather surprising. The observation of the cases which have occurred during the last eleven years in Dr. Osler's clinic has led us to believe that the drug is of value in many instances.

DR. FUTCHER.—I would like to say simply a word or two in regard to the suggestion of Hunter that pernicious anæmia may be due to the condition of the teeth. When one reads his article one is not very thoroughly convinced that his cases were really due to the involvement of the teeth. His view is that as a result of the caries of the teeth, toxic substances are formed by the bacteria present, which on being

absorbed into the blood cause a destruction of the red blood-corpuscles. He holds that the gastritis so frequently present is very often secondary to the suppurating teeth. He reported nine cases in his original paper, and in all probability there is some connection between the two conditions, but his observations require further support before being accepted. I think in this case, as Dr. McCrea suggests, it would be important to have the teeth attended to.

Contribution to the Study of the Frequency of Gall Stones in the United States. DR. MOSHER.

(See page 253.)

Diabetes Mellitus Associated with Hyaline Degeneration of the Islands of Langerhans of the Pancreas. DR. OPIE.

The pancreas, it is well known, closely resembles the salivary glands. The larger ducts are lined with high columnar epithelium which becomes lower and cubical in the smaller branches while the terminal ducts are formed by flat epithelial cells. The secreting acini are composed of high, characteristically glandular cells. Scattered throughout the organ and distinguishing it from other glands are the peculiar bodies first described by Langerhans in 1869. These consist of small polygonal, non-granular cells, which differ markedly from the ordinary secreting cells and are not arranged about a central lumen. When the blood-vessels of the pancreas are injected, corresponding to these groups of cells are seen glomeruli of dilated and tortuous anastomosing capillaries. The cells of the island form small solid columns which lie in the meshes of this capillary network. These bodies are not penetrated by the ducts and they are entirely independent of the secreting apparatus. In architecture they resemble certain ductless glands, the coecygeal and the carotid glands, the parathyroid bodies and less closely the pituitary gland, the adrenals and the thyroid. Their structure suggests that they exert some influence on the blood and are independent of the external secretion of the acini.

Experimental work has conclusively demonstrated that the pancreas bears an intimate relation to carbohydrate metabolism. When the organ is extirpated, sugar accumulates in the blood and is excreted by the kidneys. The association of lesions of the pancreas with diabetes has long been known, and in view of the experimental results a variety of destructive lesions of the gland may be regarded as the cause of the disease. Chronic interstitial pancreatitis is the most common of such lesions. Diabetes, however, does not always accompany chronic pancreatitis.

In a recent number of the *Journal of Experimental Medicine* I have described two types of chronic pancreatitis. With one variety, which may be designated interlobular, the increase of interstitial tissue is between the lobules and invades them from the periphery. In the second variety the inter-acinar, the new growth of tissue is more diffuse and penetrates between the acini. In the first the islands of Langerhans are affected by the lesion only when it has reached a very advanced grade. To this type belongs the chronic

inflammation which follows occlusion of the pancreatic duct. If the duct be obstructed by calculi or carcinoma the secreting acini are destroyed and replaced by fibrous tissue, but the islands of Langerhans remain unaffected until the sclerotic process is far advanced.

Of eleven cases of interlobular pancreatitis, in only one was diabetes present, and here the chronic inflammation which followed occlusion of the duct was so far advanced that the organ was almost entirely replaced by dense scar-like tissue in which the persisting islands of Langerhans had undergone alterations. Diabetes had been of very mild severity, and sugar had disappeared from the urine when the patient was put upon a diet poor in carbohydrates. Of three cases of interacinar pancreatitis, in two diabetes was present, while in the third the lesion of the gland was very slight and the organ was of large size, weighing 170 grammes. Where diabetes accompanied chronic interstitial pancreatitis, the islands of Langerhans were implicated in the inflammatory change; diabetes did not accompany those lesions which spared the islands.

In the same report I described a case of diabetes in which the pancreas was the seat of a very remarkable change. Throughout the gland were sharply circumscribed areas in which between the capillary wall and the parenchymatous cells hyaline material had been found. These areas in many instances corresponded in shape and size to islands of Langerhans, and nowhere in the gland were these bodies still recognizable. Not infrequently, however, the areas of hyaline degeneration were much larger and evidently represented in part at least secreting parenchyma.

In a case of diabetes which has recently come to autopsy, the pancreas was the seat of a similar hyaline change limited to the islands of Langerhans. This condition occurred in a negress, 55 years of age, who for eleven months before admission to the Hospital had suffered with severe cough. Several months after the onset of her illness she noticed that her urine had become pale and was very abundant, so that at night she was compelled to void it every hour. There were great hunger and thirst. These symptoms lasted during a part of the spring and summer, but disappeared several months before her entrance into the hospital. On admission, physical examination showed the signs of partial consolidation of both lungs and of cavities in both apices. In the sputum were numerous tubercle bacilli. The urine contained a large quantity of sugar (4 to 5.4%), although for several months she had had no symptoms indicative of diabetes. She died on the seventh day after admission; death was not preceded by coma.

At autopsy the lungs were found to be studded with tubercles, the upper lobes were consolidated, and at both apices were large cavities. Small tuberculous ulcers were present in the intestine. There were no other noteworthy lesions in the body. The pancreas was of normal size, weighing 80 grammes, and was of the usual color and consistency. Microscopic examination, however, demonstrated a lesion even more remarkable than that of the previously mentioned case.

In varying amount within almost every island of Langerhans was a homogeneous hyaline material replacing the epithelial cells. It stained deeply by acid dyes, eosin and picric acid, and in sections treated by Mallory's method for the demonstration of fibrous tissue and reticulum assumed a very conspicuous deep blue color; the reactions of amyloid were not obtained. The smallest particles of this substance were polygonal in shape and corresponded in size to the cells of the island. Transitions between the granular nucleated cells and these homogeneous hyaline particles were found. Where the process was more advanced the cells of the island were in great part or wholly transformed, and there occurred small, round or oval masses of hyaline material penetrated by the remains of capillaries whose endothelial cells finally disappear. The secreting parenchyma was unaffected by the lesion described.

In none of the cases which I had previously described was a lesion of the pancreas limited to one or other element of the gland. Where diabetes accompanied a lesion of the islands of Langerhans the secreting parenchyma was also implicated. Where diabetes was absent, the islands persisting unaltered though the secreting parenchyma was in large part destroyed, a considerable proportion of the glandular substance still remained intact. In the present case, however, diabetes followed a lesion affecting only the islands of Langerhans. It furnishes, I believe, conclusive demonstration of the inferences drawn from the preceding series of cases. Diabetes mellitus when the result of a lesion of the pancreas is caused by destruction of the islands of Langerhans and occurs only when these bodies are in part or wholly destroyed.

DISCUSSION.

DR. FUTCHER.—I would like to emphasize the great importance of this observation of Dr. Opie's. It is one of the most important on the pathology of diabetes mellitus that has been made in several years. For a good while the pancreas was supposed to be closely connected in some way with the proper metabolism of carbo-hydrates in the system. In experimental work it was shown that ligation of the pancreatic duct preventing the outflow of the pancreatic secretion into the intestine did not lead to diabetes. It was inferred that there was some internal secretion produced by the pancreas which reached the general circulation without entering the intestinal tract. A number of years ago Lépine advanced the theory that this internal secretion probably contained a ferment to which he gave the name glycolytic ferment. He believes that it has the function of causing the proper combustion of the carbo-hydrates and preventing their appearance in the urine. It is possible that these islands of Langerhans are connected in some way with the production of this ferment, if such a ferment exist. It is at least a very suggestive idea, and it seems quite conclusive from Dr. Opie's researches that the inferences drawn from his earlier work in this line were quite correct.

Carcinoma of the Male Breast. MR. WARFIELD.

(To appear in a future number.)

March 18, 1901.

The meeting was called to order by the president, Dr. Welch.

A Curious Form of Peritoneal Tuberculosis. DR. MACCALLUM.

(To appear in a future number.)

A Lipo-Myoma of the Uterus, with Exhibition of Specimen. DR. KNOX.

(To appear in a future number.)

The Advances Made in Medical and Surgical Diagnosis by the Roentgen Method. DR. CHARLES LESTER LEONARD, of Philadelphia.

(To appear in a future number.)

Monday, April 1, 1901.

The meeting was called to order by the president, Dr. Welch.

Exhibition of Medical Cases. On Hemorrhage in Chronic Jaundice. DR. OSLER.

An interesting fact in connection with diseases of the liver, associated with jaundice, is the tendency to hemorrhage. In cirrhosis of the liver, even with very slight jaundice, there may be frequent bleedings, especially to epistaxis, of which we have a case in ward now. In chronic jaundice there is a marked retardation of the blood coagulation time, sometimes even to 15 or 20 minutes, and with it there is a liability to spontaneous hemorrhages and a tendency to bleed from wounds, more particularly those of operation. Surgeons have this very painfully impressed upon them in recurring, obstinate, and even lethal hemorrhage following gall-stone operations. We have had lately four cases in the ward with jaundice and severe hemorrhages.

Case 1. Carcinoma of liver and gall-bladder. Mrs. K. had suffered with jaundice, accompanied by a great deal of pain for four months. The blood coagulation time on admission was ten minutes. A deep-seated tumor-mass of doubtful character was felt in the region of the liver. The extreme persistence of the jaundice and severity of the pain made us suspect malignant disease. On January 27 she had some slight bleeding from the gums and there was a small quantity of blood in the stools. On the 28th she bled a great deal more and was in such a desperate condition that it was thought advisable to perform a laparotomy. This was done on the following day and a carcinoma of the gall-bladder was removed. That night a severe hemorrhage occurred and persisted till death.

Case 2. You may remember that a few weeks ago I showed a remarkable case of multiple xanthelasmata and that

I referred to a second case in the house at the time but too ill to be brought down. She is now before you and illustrates in a remarkable way the feature of which I am speaking. The jaundice has existed for ten years, arising originally, in all probability, from gall-stones. The point of special interest is that she has had four attacks of hemorrhage of a very severe character, the last occurring February 18, the day before admission. For four days she had been bleeding from the nose and uterus, and at time of entrance was almost bloodless; coagulation time 14 minutes. She has steadily improved while here, the red cells having reached normal and the coagulation time has fallen to four minutes. She has gained weight at the rate of 2 pounds a week, and says she has not been so robust for some years past. The jaundice has lessened.

Case 3. Mrs. F. came in recently with a jaundice of 14 months' duration and evidences of gall-stones in the common duct. She had never had hemorrhages. Blood coagulation time was 8 minutes, but it fell gradually to $3\frac{1}{2}$ minutes and she was transferred to the surgeons and operated upon March 5. Numerous gall-stones were found in the common duct and in the gall-bladder. The day after operation there was a small hematoma in the region of the incision, and four days later she nearly bled to death. She recovered from the collapse, however, and has since done well.

Case 4. This patient was admitted in February with jaundice, nausea and a great deal of pain; coagulation time $3\frac{1}{2}$ minutes. She was transferred to the surgical side on March 8. On the day following, she had a very severe pain in the abdomen, which was followed the next day by a sudden collapse and death in a few hours. Subsequent examination showed a most extensive hemorrhage into the lesser peritoneum, the stomach and the tail of the pancreas. She had gall-stones and cancer of the gall-bladder and liver.

These cases illustrate the liability to hemorrhage in chronic jaundice and the risk in connection with operation. They show also the possibility of reducing the blood coagulation time to normal by treatment. Professor Wright, of Netley, has shown that the coagulability of the blood could be increased by calcium chloride. Subcutaneous injections of gelatin have the same effect, and we use these measures in cases of jaundice before transferring them to the surgical side.

Typhoid Spine. DR. OSLER.

This patient illustrates a very remarkable and unusual condition, which sometimes puzzles the physician. It is among the rarer sequelæ of typhoid fever. The condition was described by Gibney, of New York, as typhoid spine, and you will find in our *Studies on Typhoid Fever* an interesting series of cases. The condition follows usually a protracted attack, as in this case, which was admitted Nov. 6 and discharged Jan. 12, after a long and severe illness. He was a little nervous before leaving the hospital, but made a good recovery, which is the usual history. A month or six weeks subsequent to convalescence the patient begins to complain

of pain in the back, with stiffness, and finally develops a complete picture, as you see it here.

The patient is a robust, healthy looking fellow, of fairly good color, but you can see that he is nervous and apprehensive. He was brought into the hospital supported by two friends, and it was with the greatest difficulty that he could be induced to sit down or lie down. Any movement of the back was excessively painful, and he winced on pressure. After he was put to bed, and had the thermo-cautery and the wet packs, he improved with great rapidity, and was soon able to be up and about. He is still very nervous, and he has still slight stiffness and tenderness of the spine. These cases all present a singularly uniform picture: first, a condition of neurasthenia, often of a very marked degree; some cases become very hysterical. Secondly, stiffness of the back, so that attempts to turn or to stoop are very painful. I have known a patient to remain in bed for six weeks or more, unable to sit up or move about without agonizing pain. Thirdly, pain on pressure is usually elicited in the lower part of the back, sometimes, as in this patient, more to one side than the other, and at times directly over the sacro-iliac synchondroses. Fourthly, and this is an all-important point, the local examination is negative, there is no sign of swelling, no fever as a rule and no leucocytosis. And lastly, the patients get promptly well, or improve with great rapidity, with the use of the Paquelin and measures directed to their neurasthenic condition. It is true it sometimes takes weeks or months before a complete cure is effected.

The condition has been termed a post-typhoid spondylitis, and it is possible that in some cases there may be actual inflammation, but whatever the nature of the malady, and I must confess it is extremely obscure, I do not think there is a bone lesion similar to that which occurs so frequently after typhoid fever, and which almost invariably proceeds to suppuration. I have not met with an instance, nor do I know of one in the literature, in which suppuration has followed in any part of the spine. I have always regarded the condition rather as a neurosis, and I must say that it responds to the treatment which we employ in this class of cases.

Intestinal Dystripsy (Classification and Pathogenesis). DR. J. C. HEMMETER.

Foetal Transmission of Typhoid Fever. DR. LYNCH.

Abscess in the Abdominal Wall. Report of Cases. DR. HUNNER.

NOTES ON NEW BOOKS.

Uterine Fibromyomata, their Pathology, Diagnosis and Treatment. With 49 illustrations. By E. STANMORE BISHOP, F. R. C. S., Eng. (Philadelphia: P. Blakiston's Son & Co.)

Although the subject of uterine myomata has always been one to which the gynecologist and general surgeon have given much attention, the literature bearing on them being very extensive, this work of Bishop's is the first extensive book to ap-

pear in English, devoted entirely to the consideration of these tumors. It comprises some 300 pages, dealing with their histogenesis, symptomatology, diagnosis and treatment, and while by no means exhaustive, especially from a pathological standpoint, the author has succeeded well in "giving a comprehensive view of the subject," his object, as stated in the preface.

Bayle has estimated that myomata occur in 20 per cent of all women over 25 years of age, while Kolb states that 40 per cent of all women over 50 years, suffer from them. This very frequency makes the subject one on which the general practitioner should be well informed. Unfortunately however, many text-books give erroneous ideas, especially in regard to the treatment of these tumors, so that it is a pleasure to find a book, such as this, the recommendations of which can be safely followed.

The introductory chapter takes up in a general way the classification, life history and the more important complications.

The chapter on anatomy contains an excellent section on the vascular supply of the uterus, the relations of the pelvic organs, and the alterations which result in these relations from the development of tumors in various directions.

A concise tabulation of symptoms, which the author divides into suggestive, characteristic, and confirmatory, together with the points to be sought for in the examination of the patient, comprise a valuable chapter.

The most interesting sections are the 4th, on the development, and the 5th, on the secondary changes in uterine mesodermic tumors. A review of the literature of the histogenesis of sarcomata, myomata and telangiectatic tumors is given in the former, while in the latter, the author discusses necrosis, calcification, and inflammatory changes. He holds the view advanced by Orth and Pfannensteil, that sarcoma commences in myomata *de novo*, and is not a degeneration, as we have been taught by Virehow and Birch-Hirschfeld. Adeno-myoma is only briefly considered.

A review of the long list of medicinal remedies which have been used is then given, the authors belief being that prolonged medicinal treatment is useless.

We wish that the statements on electrical treatment, so strongly recommended by Apostoli, Keith, Playfair and others, were as decided as those in regard to medicines. "Undoubtedly in certain cases, it does produce a definite and reliable effect, while in others it is entirely useless and extremely dangerous. . . . So long as it does not blind patient and surgeon to the actual dangers of delay, in cases which ultimately require operation, so long will it be one of the really effective weapons for use against the disease." Statements with which few American surgeons will agree.

The chapter on surgical treatment is begun by emphasis on the fact that many cases require no treatment whatever. "They are best treated by masterly inactivity." The history of the evolution of the various operations is then given and several pages devoted to the internal secretion of the ovary. Myomectomy (the removal of the tumor *per se*, leaving the uterus *in situ*) is recommended whenever practicable. For hysterectomy, the author prefers the vaginal operation, when the size of the tumor permits.

The 9th chapter contains many excellent points on general technique. An exception must however be taken to the statement in regard to gloves. "Cotton gloves can be boiled or steamed before use, but it seems quite as difficult to sterilize rubber gloves, as it is to sterilize the skin. They certainly

cannot be exposed to sufficient heat to render them germ free." (*Sic!*).

The various operations are divided into (1) methods which decrease the nutrition of the tumor; (2) methods which remove the tumor alone; (3) methods which remove the uterus and the tumor; and the details of these operations reviewed.

Chapters on post-operative treatment and final results follow and an excellent bibliography is appended.

Throughout, the text has been carefully prepared and the numerous cases cited are interesting and well selected. The illustrations are fairly good but most of them have no clear detail and are lacking in plastic effect. Figures 35, 36 and 37 are excellent.

B. R. S.

Atlas and Epitome of Ophthalmoscopy and Ophthalmoscopic Diagnosis. By PROF. DR. O. HAAB, Director of the Eye Clinic in Zurich. From the Third Revised and Enlarged German Edition. Edited by GEO. E. DE SCHWEINITZ, Professor of Ophthalmology, Jefferson Medical College, Philadelphia. With 152 colored lithographic illustrations and 85 pages of text. (Philadelphia and London: W. B. Saunders & Co., 1901.) Price, \$3 net.

With the exception of von Graefe and Arlt no ophthalmologist in Europe possessed such gifts as a teacher nor left such a strong impress upon his students as Horner of Zurich. One finds his former assistants occupying high positions in ophthalmology all over the world.

As regards his industry and in a measure too as regards his other gifts his mantle seems to have fallen upon the shoulders of O. Haab who was once his assistant and who now occupies the Chair of Ophthalmology in Zurich. Haab's work is a welcome addition to our armamentarium.

Most atlases of ophthalmoscopy while they give classic examples of the different fundus affections seldom or at least to a limited extent give us pictures of the deviations or rather modifications of those pictures which are peculiarly characteristic of the different diseases.

As a matter of fact the well-known picture of albuminuric retinitis is seldom seen but we not unfrequently do see albuminuria associated with marked changes in the retina, changes which even if they are not arranged in the classic style have quite the same significance.

The author has kept this point in view throughout and we not only find the so-called typical pictures of well-known diseases but also pictures which illustrate the subvarieties and different stages of the same affection. Curious and very rare ophthalmoscopic pictures are startling but from a practical point of view they are unimportant and for this reason doubtless they occupy no space in Haab's collection.

A number of anatomical figures have been added to illustrate various microscopic conditions and this strikes us as being very appropriate and at the same time a practical departure from the ordinary run of similar works. Part first consists of about sixty pages and is nothing more than a discussion of the general principles of ophthalmoscopy and is about what we find in all text-books on the eye. Much that is said in this chapter is illumined by the comments and suggestions of the editor.

The mechanical part of the work is well done and the whole is embodied in such handy shape as will contribute largely to the success of the work.

R. L. R.

An Atlas of the Medulla and Midbrain. By FLORENCE R. SABIN, M. D. (Baltimore: The Friedenwald Co., 1901.) Pages 112.

A study of the labyrinth of the medulla by the student of medicine is ever fraught with uncertainty and misgivings on his part. The anatomy is so complex, the details of the connections of cell and nerve fibre are so complicated, that the majority shrink from obtaining, from available text-book literature, even a superficial insight into its structure.

Dr. Sabin's model of the "relay station" of the central nervous system, now elucidated by a complete commentary, was planned to meet the need for some "simple yet reliable method of aiding the students to obtain a reasonably clear idea of the organ." The text, and plates from the model, the latter from the brush of M. Broedel, fully achieve the purpose of the author.

The eight plates accompanying the volume are all well chosen, presenting clearly to the eye the gross structure of the medulla. To more particularly call attention to each nucleus of origin and fibre tract, and to impress them upon the memory, colors are used to differentiate the several parts, the effect being at once striking and artistic.

The descriptions of the various gray nodes and fibre bands are clear and comprehensive, and are sufficiently concise not to be a drain upon one's time and beget hazy ideas of the whole. Chapters V and VI upon the cerebral nerves and nuclei of origin are not only the most interesting but the most picturesque of the book.

Diseases of the Nose and Throat. By D. BRADEN KYLE, M. D., Clinical Professor of Laryngology and Rhinology, Jefferson Medical College, Philadelphia; Consulting Laryngologist, Rhinologist and Otologist, St. Agnes' Hospital. Second Edition, Revised. Octavo, 646 pages; over 150 illustrations and 6 lithographic plates. (Philadelphia and London: W. B. Saunders & Co., 1901.) Cloth, \$4 net.

A review of the first edition of this excellent book appeared in November last. In the present edition very few changes have been made beyond the correction of typographical errors. The work presents the subject of Diseases of the Nose and Throat in a concise manner, keeping in mind the needs of the student and general practitioner as well as those of the specialist. With the practical purpose of the book in mind, extended consideration has been given to details of treatment, each disease being considered in full, and definite courses being laid down to meet special conditions and symptoms. The work is very valuable.

Essentials of the Diseases of Children. By WILLIAM M. POWELL. Third Edition. Revised by ALFRED HAND, JR., Dispensary Physician and Pathologist to the Children's Hospital, Philadelphia. (Philadelphia: W. B. Saunders & Co., 1901.)

To condense the present knowledge of any important division of medicine into a volume of two hundred and fifty small pages and not omit much that is essential would be almost impossible and this is true of the present subject.

As the author points out much too little is said of diet and general hygiene to convey the accurate knowledge their importance demands—three and one-half pages being given to "Infant Feeding."

The discussion of the acute infectious diseases is quite as good as the limited space will permit—though it is hardly safe to describe scarlet fever as a "somewhat contagious disease."

On the whole this third edition of Dr. Powell's book is quite up to the standard of books of its class—but it is difficult to see in just what these systems of questions and answers are of benefit to either students or practitioners. The book is well made and unusually free from typographical errors.

R. A. U.

Students' Edition, a Practical Treatise of Materia Medica and Therapeutics, with special reference to the Clinical Application of Drugs. By JOHN V. SHOEMAKER, M. D., LL. D., Professor of Materia Medica, Pharmacology, Therapeutics, and Clinical Medicine and Clinical Professor of Diseases of the Skin in the Medico-Chirurgical College, of Philadelphia, etc. Fifth Edition. Thoroughly Revised. Pages vii-770. Extra Cloth, \$4 net. (Philadelphia: F. A. Davis Co., 1901.)

In this fifth edition of Dr. Shoemaker's well-known treatise the pages have been thoroughly revised and many new subjects added, but inasmuch as it is designed especially for students, "nothing is included beyond a description of those drugs and preparations which are official in the Pharmacopœias of the United States and Great Britain." Dr. Shoemaker has happily expressed the doses in the metric system, adding their equivalents in the English system. This seems to be a very wise procedure inasmuch as students can only be gotten to write their prescriptions in metric terms when they have to learn their doses in that system. Our Pharmacopœia has already committed itself to this system and it is but the proper sequence that physicians should write their prescriptions in it.

The work is divided into two parts. Part one consisting of seventy-four pages, deals with certain general considerations of the subject introductory to the more detailed study of the various drugs and their uses which follows in the second part. These general considerations consist of definitions, the botanical orders and names of the various medicinal plants, a few pages upon pharmacy and methods of making the various pharmaceutical preparations; prescription writing; methods of administration of drugs; poisons and their antidotes; etc. Though briefly written, it contains many excellent suggestions. Some exception may be taken to the author's use of the term pharmacology, signifying the science of drugs, a study of their natural history, their physical and chemical characters, and the various methods of compounding and dispensing them. Most authors prefer to limit this term definitely to the study of the physiological action of drugs, and it seems to us that this is decidedly a better word to apply to that subject than the one here suggested of "Pharmacodynamics."

In part two the various pharmaceutical products are taken up in alphabetical order. Each is considered under several headings. First its preparations are named; then under "Pharmacology" a description of the drug is given, its source, its physical characteristics, its solubility, reaction, etc.; under "Physiological action" the substance is spoken of in relation to its effects upon animals and man. Next follows the heading Therapy where its usefulness in medicine is expounded; here frequently a number of prescriptions are added. Part two embraces about 650 pages, closely written, and the numberless products, many of which are of so little use in medicine, yet so fully described, make it rather a forbidding book to place

in the hands of the student. At the same time the important subjects are well considered and if the paragraphs upon the therapeutic value of drugs are somewhat optimistic and hopeful, still it seems to be a very useful reference handbook to the student who desires to have a full pharmacopeial armamentarium for his practical work. Nothing is said of such useful therapeutic measures as hydrotherapy, climate, serotherapy, etc., the book being absolutely limited to the consideration of drugs and their administration.

It is to be hoped that some time there will arise a courageous author who will write a book upon treatment in which only really useful remedies, numbering probably over fifty, will be spoken of in such a way that the future student may learn to handle them effectively and scientifically, and the great burden of remembering, even of looking through the scores of utterly antiquated and useless preparations will be avoided.

H. B. J.

A System of Physiologic Therapeutics. Edited by SOLOMON SOLIS COHEN, A. M., M. D. Vol. I, Electrotherapy, by GEORGE W. JACOBY, M. D. In two books. Book I, Electrophysics. 163 illustrations. (Philadelphia: Blakiston's Son & Co., 1901.) pp. xv-242.

The volume at hand is the first of a series which will compose a system of physiologic therapeutics, embracing eleven octavo volumes, devoted to the consideration of measures other than medicinal, which experience has shown are beneficial in the cure and prevention of disease. The appearance of such a system of medicine is timely as no author or authors have until now, gathered together in one volume or series of volumes, in English, these methods which are so very important in the treatment of disease. The statement made at the sub-heading of the title page really covers the scope of the work, "The practical exposition of the methods other than drug giving useful in the treatment of the sick." This first volume by Dr. Jacoby, who is so well fitted to write upon the topic, is devoted to electrotherapy and is to be divided into two parts or books, Book I being given up to the physical aspects of electricity with a description of the various forms of apparatus that physicians are likely to use. The further volumes as the announcement and the "foreword" of Dr. Cohen state, will consider Climatology and Health Resorts; Nursing and Care of the Sick; Diet; Hydrotherapy; Serotherapy; etc.

There is surely room for just such a set of books. We have been too prone to think that we were teaching therapeutics sufficiently when we taught our students the old *materia medica* and the use of mere drugs, forgetful and careless of the importance of the therapeutic value of the methods of which this series of books will speak. That the necessity of this line of teaching has already come into the minds of some men may be seen in Dr. Lauder Brunton's volume entitled "Lectures on the Actions of Medicines," in which he not only writes upon various pharmaceutical products, but also devotes many pages at intervals through the book to diet, massage, counter irritants, hydrotherapy, poultices, etc.; and to the minds of still others, as may be seen in the announcement of one of our medical schools, where in speaking of its course upon Practical Therapeutics, it states that the course teaches among other things "the administration of practical therapeutic measures, the use of massage, the preparation and useful forms of diet, the care of patients considered from the nursing point of view, the treatment of various emergencies, of special

diseases by climate, rest, and other practical procedures." This course as advertised then practically epitomizes the work which Dr. Cohen will embrace in his larger system of physiologic therapeutics. The volume before us opens with a foreword by Dr. Cohen on Therapeutics without Drugs, and comprises an argument for the need of such a series of books. Here he justifies briefly the term "physiologic therapeutics" by referring to Mr. Herbert Spencer's definition of life, maintaining that the subjects to be treated in the forthcoming volumes merely assist in aiding nature to preserve that normal equilibrium within its environment which constitutes health, and therefore become physiologic in their curative action.

The use of drugs, on the other hand, for therapeutic purposes he would term "artificial," inasmuch as through them there is introduced into the organism substances ordinarily absent therefrom and foreign to its composition. It is not his purpose, however, to antagonize the latter therapeutic measures in the least, for he admits "having a robust faith in the power of good of the right drug, given in the right dose, at the right time."

That every one will subscribe to all of Dr. Cohen's conclusions I am inclined to doubt; for instance: on page ix there is found the following paragraph: "The pathologic influence of emotion is well shown in the evolution of exophthalmic goiter and in the protean manifestations of hysteria, etc., etc." This seems so far as the former disease is concerned rather a bold statement, and I should be surprised to find that many would admit the basis for the production of exophthalmic goiter was to be found in an emotion.

The volume is devoted through 225 or more pages to a description of the terms used in electricity, the physical explanation of electricity, the various methods of producing it, and the arrangements for controlling, measuring, and applying it. The text is very fully illustrated and the subject presented so clearly that one with little conception of the real nature of the subject may get a fair idea of it. There is gathered together in this one volume knowledge which one could otherwise only acquire through numerous books upon physics and medical electricity, and to that extent it is extremely useful. Nothing, however, in this part of Volume I is said upon the therapeutic value of electricity; that topic, doubtless, being reserved for part two of Volume I.

It seems questionable whether many medical men will care to learn the various facts in regard to electricity which are here set forth. It is knowledge for the electrician rather than for the every-day practising physician; knowledge which is necessary for one establishing an electro-therapeutic institution, but not for the man who applies the electrodes for diagnostic or therapeutic purposes. From a mechanical point of view the book is admirably gotten up. It is a credit to its makers. The paper is heavy and fine; the printing clear, type of good size, and well spaced, and the illustrations excellent.

It is greatly to be hoped that the completed work will not become so voluminous as to lose its general usefulness. Completeness with brevity, conciseness with lucidity should be the aim of all medical editors.

H. B. J.

Anomalies of Refraction and of the Muscles of the Eye. By FLAVEL B. TIFFANY, A. M., M. D. Author's Fourth Edition. (Kansas City, Mo.: Hudson-Kimberly Publishing Co., 1900.)

It was Job, we believe, who wished that his adversary had written a book. If Dr. Tiffany has any adversaries, or, at all

events, any that are inclined to be critical, he has unquestionably afforded them, in the publication of the book we are called upon to review, such an opportunity as the great lamenter must have had in mind when he expressed this wish.

As the "reviews" which accompany the book state, it is "elaborately illustrated"; and it contains unquestionably, much useful information upon the subject of which it treats; but that it has been "carefully revised," and the "few errors [of the earlier editions] corrected," as is claimed in the publisher's notice, we are hardly inclined to concede. Indeed, we have seldom glanced through a book that seemed to be so sorely in need of what this one is supposed to have just received—"careful revision," and though a "few errors" may have been corrected there are a host of others still awaiting elimination.

One of the first of these to attract our attention occurs in the preface, and seems to have been handed down, without detection, from the first to the present, fourth, edition. "Many instruments and *apparati*,"¹ the author—unmindful of his declensions—tells us, "have been invented," etc. Whether heterophoria and ametropia deserve to be characterized, as they are in another part of the preface, as "vast subjects . . . still wrapped in a halo of uncertainties" is, of course, a matter simply of taste; and the same observation applies to this, which we find on p. 69: "it is only when there is an appreciable variation in the curvature that the eye is stigmatised (sic) astigmatic."

The definition on p. 65 of an ametropic eye as one which cannot focus parallel rays of light, "without an effort of accommodation," is distinctly erroneous; for it is evident that ametropia, so defined, would not include myopia. The statement on p. 107 that "more or less choroidal blood-vessels may be seen through the retina, especially in a dark-complexioned person," is open to criticism upon more grounds than one; but we shall content ourselves by pointing out that it is in blondes, as a rule, that the choroidal vessels are most plainly seen, and in brunettes that they are least distinguishable.

On p. 156 we read, with some surprise, "the hyperopic eye is an undeveloped eye, with sight not up to the normal standard of distinctness for either near or distant objects"; but,

notwithstanding this unequivocal statement, we are told on the following page that "the hyperopic eye of a moderate degree with good power of accommodation may have the normal amount of vision"; and, again, on p. 158, that "hypermetropes with less than 3.50 D., with good accommodation, as a rule, have $\frac{20}{xx}$ or normal vision." On p. 159 we learn that "the strongest glass that they [hypermetropes] require without the use of a mydriatic indicates the *manifest* hypermetropia." It is hardly necessary to point out that most young hypermetropes, though a considerable part of their error of refraction may be made manifest by painstaking effort require no glass at all to obtain normal distant vision. Quite as surprising is the statement on the same page that "the manifest [hypermetropes] is *usually* apparent without a mydriatic."

Space does not permit us to call attention to all of the shortcomings which have arrested our attention in looking over the pages of Dr. Tiffany's book; but, as examples of many others, the following may be cited: "Hypermetropia can be corrected, but may not be *entirely* cured" (p. 168). "Frequently we have what is known as a *spasm of accommodation*, which causes partial paralysis or paresis of the ciliary muscle" (p. 169). "It is now a conceded fact that hyperopia is often a primary cause of . . . trachoma" (p. 170). Possibly "*hyperboloidal* glass," on p. 209, is a printer's error; but, if not, it is evident there is still virgin soil for Dr. Gould to delve in. "It is much better to under-correct [in performing a tenotomy] and have to repeat the operation than to over-correct and be obliged to advance the *opposing* (sic) muscle." (p. 247).

Far be it from us to belittle the ill effects of eye strain, whether due to refraction or muscular anomalies; but we cannot but feel that the author has drawn an unnecessarily lurid picture in thus describing the consequences of heterophoria: "Life becomes a burden; despondency, melancholia, insomnia, and suicide may be the end" (p. 230). And again, "in neurotic and feeble patients the muscular errors or insufficiencies may produce aphoria, diarrhoea, pains of the ovaries . . . and insanity even" (p. 233).

We are not surprised to learn, from the "reviews," to which allusion has been made, that Dr. Tiffany's treatise is highly thought of by jewelers and opticians and by the Philadelphia "Optical College."

S. T.

¹ The italics here and in many other places in this review are our own.

STUDIES IN TYPHOID FEVER.

SERIES I-II-III.

The papers on Typhoid Fever, edited by Professor William Osler, M.D., and printed in Volumes IV, V and VIII of The Johns Hopkins Hospital Reports have been brought together, and bound in cloth.

The volume includes thirty-five papers by Doctors Osler, Thayer, Hewetson, Blumer, Flexner, Read, Parsons, Finney, Cushing, Lyon, Mitchell, Hamburger, Dobbin, Camac, Gwyn, Emerson and Young. It contains 776 pages, large octavo, with illustrations. It gives an analysis and study of the cases of Typhoid Fever in The Johns Hopkins Hospital for the past ten years.

The price is \$5.00 per copy. Only a few copies of the volume are on sale. Those wishing to purchase should address their orders to the JOHNS HOPKINS PRESS, BALTIMORE, MARYLAND.

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THE HISTORY AND WORK OF THE SARANAC LABORATORY FOR THE STUDY OF TUBERCULOSIS.¹

BY E. L. TRUDEAU, M. D., Saranac Lake, N. Y.

GENTLEMEN :—I feel much as a scout, who had been doing duty alone on some frontier for many years, might feel when suddenly brought into the presence of a well organized army, and I assure you I appreciate the privilege of addressing you. I must apologize for talking of my own work, but the necessities of the situation make this more or less unavoidable. My experiences may prove an encouragement, perhaps, to those of you who are to locate at distant points, as demonstrating the possibility of doing scientific work in remote regions, far from the centres of learning, and they may prove of interest to a Society such as yours as describing the foundation of the first laboratory in this country devoted to researches in tuberculosis.

I had from the first many difficulties to contend with; no health, no scientific training, no apparatus, no access to books, and was situated forty-two miles from a railroad, in a primitive forest, where I had gone in search of health.

My inspiration was Koch's paper on the Etiology of Tuberculosis, of which I read an extract in a medical journal in 1883, and which was translated into English and sent me by a patient. In some of the short visits I was enabled to make to New York, Dr. Prudden taught me how to stain the bacillus, and the first principles of bacteriology, and I taught myself the rest as best I could.

My laboratory was a very small room in my house, in which, during the intense cold of winter, water generally froze at night, in spite of my best efforts, as we had no coal in Saranac Lake in those days, and the wood stove could not be counted upon to burn all night. I had no apparatus but my microscope. With Dr. Koch's paper as a guide, I succeeded, however, in growing the tubercle bacillus in a homemade thermostat, which had no regulating apparatus, and which was heated by a small kerosene lamp only. In order to protect this from the violent changes of temperature, which occurred principally at night, I had enclosed it in a series of wooden boxes, the doors of which could be opened

¹ Read before The Laennec, a Society for the Study of Tuberculosis at the Johns Hopkins Hospital, May 1, 1901.

or closed at will, according to the intensity of the cold out of doors. But on very cold nights I was obliged to get up in the night to make a fire in the stove in order to prevent too violent changes of temperature in my little oven.

With these primitive arrangements, after many failures, I obtained the tubercle bacillus in pure cultures, being, I believe, the second observer in America to do this; Dr. Sternberg, while himself located on the frontier, in a far distant military post, having succeeded in accomplishing this nearly a year before I did. With these cultures I repeated all Koch's inoculation experiments.

My guinea-pigs had to be kept in a hole under ground heated by a kerosene lamp, this being the only spot in Saranac Lake where they could escape freezing at night.

My first publication,² in 1886, was a record of experiments demonstrating the infectiousness of bacillary sputum, and the harmlessness of expectoration free from bacilli taken from a patient supposed to have consumption.

In 1886 I also studied the influence of extremes of environment on the course of inoculation tuberculosis, and published the results in a paper entitled "Environment and its Relation to Bacterial Invasion in Tuberculosis."³ Many of my inoculated rabbits allowed to run wild on an island recovered, or developed only a localized disease, while those placed under the most unhygienic conditions I could devise, all died of tuberculosis within three months. The results of this research increased my confidence in the influence of a favorable environment on the course of the disease, and confirmed my faith in the value of the sanitarium and open-air method of treating tuberculosis, of which I was then making a practical application in the establishment of the Adirondack Cottage Sanitarium.

During the same week in which Koch's announcement of the discovery of tuberculin and of his hopes as to its specific curative action on tuberculosis, was flashed across the ocean and created in medical circles an excitement which has never been equaled, I published in the *Medical Record*⁴ an article describing my attempts at the production of artificial immunity in animals by the injections of sterilized and filtered liquid cultures of the tubercle bacillus (tuberculin), and my failure to obtain any appreciable degree of immunity by this method.

Shortly after this time Dr. E. R. Baldwin came to Saranac Lake in search of health, and while at the Sanitarium began to help me with my experiments. How efficient a helper he has proved his own published work testifies, and the Laboratory at Saranac Lake owes much to his unselfish devotion to science.

About this time, while ill in New York, my house burned to the ground, the fire having originated during the night from the explosion of the kerosene lamp of the thermostat in my little laboratory, and everything in the house and laboratory proved a total loss. Two days after the fire I

received from Dr. Osler a brief note, which shows that his great reputation should not be limited to his attainments as a physician, but that he may lay claim also to some reputation as a prophet. The entire substance of the note was as follows:

"DEAR TRUDEAU:—I am sorry to hear of your misfortune, but, take my word for it, there is nothing like a fire to make a man do the Phoenix trick."

Dr. Osler's prophecy very soon began to be realized. A friend and patient of mine, Mr. George C. Cooper, called on me the day after the fire, and after expressing his sympathy, told me that as soon as I was well enough he hoped I would return to Saranac Lake and build a suitable laboratory; one that could not burn down. That he wanted me to build the best I could plan for the purpose, and that he would pay for it. The photographs I show you illustrate how I availed myself of his generous offer.

The building is of cut stone, slate, glazed brick, and steel, completely fireproof, lit by electricity, heated by hot water, supplied with its own gas machine for the thermostats, Bunsen burners, and sterilizers, and furnished with every appliance for bacteriological and chemical work. It has a library which was donated by the late Mr. Horatio Garrett, of Baltimore, while the continuance of the experimental work so far has been made possible through the generosity of the late Mr. George Cooper, Miss Cooper, Mr. John Garrett, Mrs. A. A. Anderson, and others, who from time to time have given sums of money to defray the necessary expenses. It is purely a research laboratory, sells no products, and has now a legal standing, having been incorporated lately as the Saranac Laboratory, according to the laws of the State of New York. It has as yet no endowment, and is still dependent on the efforts of its founder for the funds necessary for its maintenance, but will, I hope, some day be endowed.

While the Laboratory was in process of construction a small addition to my stable was hastily built, and served as a temporary laboratory, in which for a year the work, thanks to the generosity of Mrs. Robert Hoe, was continued.

Much time was at first naturally enough devoted to the self-education of the staff of the Laboratory, to the study of the various culture-media proposed from time to time, and to perfecting our technic. A good deal of the work of the Laboratory has been given to testing experimentally all proposed specific methods of treatment and all consumption cures. The outlook, at first, seemed to tend toward the application of germicidal substances, and many experiments, which all proved barren of results, were made in this direction. We soon learned that the tubercle bacillus bore "cheerfully" a degree of medication which proved fatal to his host. We found that creosote, iodoform, sulphureted hydrogen, hydrofluoric acid, essence of peppermint, and other germicides proposed as cures, while they had no influence on the tuberculous process, often tended to shorten the lives of the treated animals. The publication of these researches, however, had some influence in disproving the claims of these

² American Journal of Medical Sciences, October, 1885.

³ American Journal of Medical Sciences, July, 1887.

⁴ Medical Record, November 22, 1890.



Saranac Laboratory for the Study of Tuberculosis. Built in 1894.



Interior of Saranac Laboratory for the Study of Tuberculosis.

specifics, and in preventing to a certain extent their more general application to the treatment of the human subject.

The next phase of our work was that which was devoted to attempts at the production of immunity by injections of sterilized attenuated cultures, and by the study on animals of the influence of treatment with toxins derived from the bacillus, and modified according to various methods proposed.

The claims made for the various tuberculins put forth by Koch, Hunter, and others, Klebs's antiphthisin and tuberculoedin, and Koch's T. R. tuberculin, as well as the different serums said to contain antitoxines capable of neutralizing the toxins of tuberculosis, were all tested in turn in many experiments, while for several years Dr. Baldwin and I, by various methods, attempted to produce a serum from rabbits, sheep, and asses, in which we could demonstrate the presence of antitoxine. Neither our serums nor any of those proposed by other experimenters were found capable of saving the tuberculous guinea-pig from a fatal dose of tuberculin.

At the time Koch published his paper on T. R. tuberculin, a study of some of the first bottles imported was made by Dr. Baldwin and myself, and demonstrated in this material the presence of living tubercle bacilli capable of infecting guinea-pigs, and enabled me to avoid the use of this substance at the time in the treatment of patients at the Sanitarium. No doubt the publication of our observations also prevented its general use until the defects in the technique of its manufacture had been remedied.

The tuberculin test and the mechanism of the tuberculin reaction have formed the subject of many of our studies, which have tended to demonstrate the reliability of the tuberculin test, and its apparent freedom from dangerous after-effects, and which have helped to throw some light on the mechanism of this reaction.

The studies made by Dr. Irwin H. Hance of the dust taken from all the buildings at the Sanitarium, showed that, with one exception (in a cottage in which a patient had been reported for expectorating on the floor), the dust tested was absolutely free from infectious properties, and this afforded experimental evidence that the methods adopted in the institution, to protect the patients from re-infection, were efficacious.

Dr. Baldwin has recently pointed out the possibility of infection of the hands of consumptives, and demonstrated the presence of living tubercle bacilli on the hands of patients using handkerchiefs, and their absence generally from the hands of Sanitarium patients who made use of the paper euspidors.

Some of the papers published by my co-workers from the Laboratory have been as follows:

1. The Effect of Peppermint Inhalation on Experimental Tuberculosis. E. R. Baldwin. New York Medical Journal, May 18, 1895.

2. Effect of Antitubercle Serum in Experimental Tuberculosis. S. W. Hewetson. New York Medical Journal, Nov. 9, 1895.

3. A Study of the Infectiousness of the Dust in the

Adirondack Cottage Sanitarium. Irwin H. Hance. Medical Record, December 28, 1895.

4. A Gift of Philanthropy to Science (The Saranae Laboratory for the Study of Tuberculosis). E. R. Baldwin. Scientific American, March 6, 1897.

5. Infection from the Hands in Pulmonary Phthisis. E. R. Baldwin. Philadelphia Medical Journal, Dec. 3, 1898.

6. Preliminary Communication on the Bio-Chemistry of the Bacillus Tuberculosis. P. A. Levene. Medical Record, Dec. 17, 1898.

7. A Case of Lymphatic Leukemia Combined with Pulmonary Tuberculosis. E. R. Baldwin and J. A. Wilder. American Journal of the Medical Sciences, June, 1899.

8. The Conditions of Tuberculous Infection and Their Control. E. R. Baldwin. Yale Medical Journal, March, 1900.

9. The Results of Sanatoria and Special Hospital Treatment in Pulmonary Tuberculosis. H. McL. Kinghorn. Montreal Medical Journal, July, 1899.

10. Some Retinal Complications in Chlorosis. H. McL. Kinghorn. Montreal Medical Journal, January, 1900.

11. Symptoms of Renal Tuberculosis. H. McL. Kinghorn. Montreal Medical Journal, March, 1901, besides twenty papers by myself, the titles of which I will spare you.⁵

⁵ Publications by E. L. Trudeau, as follows:

1. An Experimental Research upon the Infectiousness of Non-Bacillary Phthisis.—Amer. Journal of the Med. Sciences, October, 1885.

2. Environment in its Relation to the Progress of Bacterial Invasion in Tuberculosis.—Amer. Journal of the Med. Sciences, July, 1887.

3. Hydrofluoric Acid as a Destructive Agent to the Tubercle Bacillus.—Medical News, May 5, 1888.

4. Hot-air Inhalations in Pulmonary Tuberculosis.—Medical News, September 28, 1889.

5. Some Cultures of the Tubercle Bacillus, Illustrating Variations in the Mode of Growth and Pathogenic Properties.—Transactions of the Assoc. of American Physicians, 1890.

6. An Experimental Study of Preventive Inoculation in Tuberculosis.—Medical Record, November 22, 1890.

7. The Treatment of Experimental Tuberculosis by Koch's Tuberculin, Hunter's Modification, and other Products of the Tubercle Bacillus.—Medical News, September 3, 1892.

8. Results of the Employment of Tuberculin and its Modifications at the Adirondack Cottage Sanitarium.—Medical News, September 10, 1892.

9. Eye Tuberculosis and Anti-tubercular Inoculation in the Rabbit.—New York Medical Journal, July 22, 1893.

10. A Report of the Ultimate Results Obtained in Experimental Eye Tuberculosis by Tuberculin Treatment and Anti-tuberculous Inoculation.—Medical News, September 29, 1894.

11. A Chemical and Experimental Research on "Antiphthisin" (Klebs). (By E. L. Trudeau and E. R. Baldwin).—Medical Record, December 21, 1895.

12. Sanatoria for the Treatment of Incipient Tuberculosis.—New York Medical Journal, February 27, 1897.

13. The Tuberculin Test in Incipient and Suspected Pulmonary Tuberculosis.—Medical News, May 29, 1897.

14. The Need of an Improved Technique in the Manufacture of Koch's "T. R." Tuberculin. (By E. L. Trudeau and E. R. Baldwin).—Medical News, August 28, 1897.

15. Remarks on Artificial Immunity in Tuberculosis.—British Medical Journal, December 25, 1897.

16. Experimental Studies on the Preparation and Effects of Anti-

Most of my own work has been devoted to the study of methods which might tend to produce artificial immunity, and has generally proved barren of definite results. All my attempts at inducing artificial immunity by the methods claimed by others to have been successful in immunizing guinea-pigs and rabbits were also negative. I learned by practical experience that toxine immunity and bacterial immunity in tuberculosis do not go hand in hand. While I could accustom my animals, by gradually increased doses at intervals, to bear without apparent injury, amounts of tuberculin and other toxic products of the tubercle bacillus which at first would have proved rapidly fatal, I found that this toxine immunization did not protect the animal against the invasion of his tissues by the bacilli when subsequently inoculated with them. The only observation I made from all this work which was in the least encouraging was obtained by preventive inoculations of cultures attenuated by many years of continuous growth on artificial media, and my results along these lines confirmed those of De Schweinitz.

By prolonged growth a culture is obtained which is not in the majority of cases fatal to rabbits, and only relatively so to guinea-pigs, many animals living over a year after the protective inoculation, and showing then only evidences of slight and localized tuberculosis. When reinoculated with virulent bacilli, guinea-pigs thus protected live about four times as long as the controls, though they all ultimately die. In rabbits thus vaccinated, and subsequently reinoculated with virulent tubercle bacilli, in the anterior chamber of the eye, the reaction produced by the virulent germs is very different from that noticed in the controls. In the controls, the introduction of the virulent bacilli in the anterior chamber produces at first little apparent irritation, and a couple of days later the eye shows no inflammatory reaction, and looks about normal. Little by little, however, tubercles begin to develop, and the conjunctival vessels become turgid, the cornea opaque, the intraocular pressure increases, and the eye goes on to more or less complete destruction. In the vaccinated animals, on the contrary, the virulent inoculation is almost at once followed by a violent inflammatory reaction, intense vascular congestion, and cloudiness of the cornea, which little by little subsides, at just the time when the eyes of the controls are rapidly getting worse. The tuberculous process in many instances seems aborted, and the eye restored, if not to its original integrity, at any rate with but little permanent destruction of the tissues involved. This

toxins for Tuberculosis. (By E. L. Trudeau and E. R. Baldwin.)—*Amer. Journal of the Med. Sciences*, December, 1898, and January, 1899.

17. The Adirondack Cottage Sanitarium for the Treatment of Incipient Pulmonary Tuberculosis.—*The Practitioner*, February, 1899.

18. The Present Aspect of Some Vexed Questions Relating to Tuberculosis, with Suggestions for Future Research Work.—*Johns Hopkins Hospital Bulletin*, No. 100, July, 1899.

19. The Sanitarium Treatment of Incipient Pulmonary Tuberculosis and its Results.—*Medical News*, June 2, 1900.

20. The First People's Sanatorium in America for the Treatment of Pulmonary Tuberculosis.—*Zeitschrift für Tuberkulose und Heilstättenwesen*, vol. 1, No. 3, 1900.

does not take place in all animals, but in the greater proportion of them.

The encouraging feature of these results lies in the fact that some influence has been produced by the preventive inoculations (which usually are best made intravenously), so that the reaction of the tissues to the test inoculation is not the same as in the controls. This peculiar reaction of the tissues to the test inoculation would seem to be due to a certain degree of acquired immunity, as in other bacterial diseases in which artificial immunity can be produced, as in anthrax, we find a violent local reaction of the tissues in the vaccinated animals; a reaction which seems to abort the occurrence of general infection, while in the controls the local reaction is wanting, and the disease runs an uninterrupted course.

Throughout all these years, the results obtained in the Laboratory have been applied practically to the development and perfecting of the sanitarium treatment, and have given us a rational basis for the methods adopted there. The demonstration of the favorable influence of environment on the course of the experimental disease; of the actual protection from infection afforded by the methods adopted at the Sanitarium to this end; of the danger of hand infection by the handkerchiefs of consumptives; of the necessity of testing thoroughly, on animals, any specific method of treatment proposed before making use of it in the human subject, as evidenced by our experience with T. R. tuberculin; of the value of the tuberculin test in the detection of the disease, and its relative freedom from danger as shown by the experimental disease in animals, are all examples of the application of knowledge gained in the Laboratory, to the practical improvement of our methods of dealing with the disease in the human subject.

While the modern sanitarium represents the practical application of what we have learned and already know, the laboratory represents what we still hope to accomplish. It is to the laboratory and to research work that we must look if we are to advance in our struggle against tuberculosis; and the importance of forming such societies as yours, and of founding laboratories for research, where facilities for original work are at hand, and where, if need be, the living expenses of the workers may be defrayed, cannot, in my opinion, well be exaggerated.

In conclusion, allow me to bring to your attention, briefly, some of the more interesting researches as yet unpublished, which have been carried out at the laboratory this winter, principally by Doctors Levene and Baldwin, and which were made possible by the generosity of Mrs. A. A. Anderson.

Dr. Phoebus A. Levene, with the assistance of Dr. E. R. Baldwin, who furnished him with the enormous quantity of germs necessary for his chemical analysis, set himself the task of making what may be termed a chemical dissection of the tubercle bacillus. Much work on the chemistry of the tubercle bacillus has been done already by Behring, Hammerschlag, Hoffman, De Schweinitz, and Ruppel. As a result of Dr. Levene's work I show you in these flasks the various

substances which he has thus far been able to isolate from the dried and crushed germs. The first flask contains a coloring matter, an alcoholic extract, of the washed, dried, and powdered bacilli. That this coloring matter is peculiar to the tubercle bacillus seems to be indicated by the fact that a few drops of it added to a glass of water give the same opalescent, yellowish green hue which is noticed in cultures growing on transparent liquid media.

He also separated a peculiar fat, or wax-like substance, which I now show you, and which forms thirty per cent. of the body substance of the bacillus. When the various component parts of the bacillus are stained, this is the only one which holds the stain in the presence of acids. It does not seem to be a toxine which causes the fever, since Dr. Baldwin demonstrated that animals inoculated with bacilli freed from fat react to tuberculin in the usual way.

Dr. Levene also separated three nucleoproteids which have different coagulation points. From these he obtained a nucleic acid, which I now show you, and which he found to contain more phosphorus than nucleic acid derived from other animal and vegetable substances which he tested. The nucleo-proteids of the tubercle bacillus are probably the toxic agent, or at least one of the toxic substances, contained in the bacilli. This was demonstrated in a set of experiments I will refer to again, where the toxicity of tuberculin was shown to be destroyed by those ferments which are known to be specially active in splitting up nucleoproteids.

Besides these substances, Dr. Levene found a glycogen, or a glycogen-like substance, which is contained in this small flask. This is the first time, to my knowledge, that this substance has been demonstrated in the tubercle bacillus, though the presence of carbohydrates has been suspected as a necessary source of energy.

He also studied the chemical differences in cultures grown on different media, in virulent and less virulent cultures, to determine the relation the chemical composition of bacteria might bear to their virulence. Comparative studies were made of bacilli grown on ordinary bouillon, and on a synthetic medium described by Proskauer and Beek, containing chiefly phosphates, mannit, and glycerin. Results show that more fat and a larger amount of proteid and free nucleic acid could be obtained from bouillon than from mannit cultures, and it would appear that toxic properties of bacillus are probably related to the nucleic acid and its combinations which they contain.

Another interesting set of experiments by Dr. Levene and Dr. Baldwin proved that the toxins of tetanus, diphtheria, and tuberculosis, are all destroyed by digestion with trypsin, and the first two by pepsin and papain also. When thus treated, tenfold fatal doses were harmless. Tuberculin could not be destroyed entirely by peptic digestion, and it is probable from this fact that it is a nucleo-proteid, this group of proteids being more resistant to pepsin.

THE PREVENTION OF TUBERCULOUS DISEASES IN INFANCY AND CHILDHOOD.¹

BY S. A. KNOPF, M. D., New York City.

Before entering my subject I desire to express my most heartfelt thanks to your Professors, Welch and Osler, who honored me with the invitation to deliver these lectures before you. To lecture to an audience composed of students and the post-graduate class of Johns Hopkins Medical School, which to-day stands as an example of what is understood to be the highest type of the medical department of a university, not only in this country but also abroad, is a privilege which, I assure you, I appreciate most highly.

As the title of my address indicates I have chosen to discuss before you to-night the Prophylaxis of Tuberculosis During Childhood. The importance of this subject I hardly need to emphasize, for the prevention of tuberculosis in children is one of the most essential factors in the solution of the tuberculosis problem.

You know of the prevalence of this scourge in the human race. Everyone of you knows some family in which one or several members are suffering from this disease, and others in which for two or three generations it has been considered

the family affliction, are not rare. The members of those unfortunate families are very often spoken of as having inherited consumption or phthisis pulmonalis.

Let us, for a moment, summarize what we really know of a direct hereditary tuberculous disease. Bacillary transmission, coming directly from the paternal side through sperm, has been experimentally demonstrated. Clinically, however, the cases are exceedingly rare. According to Lartigau² there are only four reported cases, and even in these it was possible that there was hereditary predisposition with subsequent bacterial infection. Benda thinks spermatozoa incapable of transporting immotile bacilli. Walter³ examined microscopically 230 different preparations from testicles and 63 from prostate glands, coming from 21 patients who had died of pulmonary tuberculosis, and could not find a single bacillus in any one of them.

The extreme rarity of primary genital tuberculosis in vagina or uterus seems the best clinical evidence that direct

¹Lecture delivered before the Senior and Post-graduate Classes of Johns Hopkins Medical School, May 28, 1901.

²"Congenital Tuberculosis," Twentieth Century Practice of Medicine, vol. xx.

³Cornet, "Die Tuberkulose," Berlin, 1899.

paternal bacillary transmission of tuberculosis practically does not exist.

Maternal bacillary transmission, on the other hand, can take place through the placenta and perhaps even through the ovum. Forty such cases of indisputable congenital tuberculosis traceable to maternal origin are now on record. This number, however, is infinitesimally small compared with the number of authentic cases where the child of a tuberculous mother has been carefully examined without finding the slightest trace of tuberculous disease, either clinically, bacteriologically, or pathologically.

Straus,⁴ who has made extensive experiments in this direction, repeatedly transplanted portions of the various organs of a fetus from a mother in the last stages of consumption into guinea-pigs and never succeeded in producing tuberculosis in these animals. Von Leyden⁵ failed likewise in his experiments to inoculate tuberculosis with organs taken from a child which had died a few minutes after birth and which had a consumptive mother. Noeard,⁶ who only experimented with animals, took the organs of 32 fetuses from four tuberculous rabbits and eight tuberculous guinea-pigs, and inoculated 32 guinea-pigs, all with negative results.

Thus it seems to us that we might consider direct bacillary transmission, even from the maternal side, so exceedingly rare as to leave it outside of consideration in studying how to prevent tuberculosis in childhood. Let us rather assume two cardinal points; first, that tuberculous infection contracted in whatever way during infancy or childhood comes from without and not from within. Secondly, that there may, however, exist a hereditary predisposition to tuberculosis. How this predisposition is brought about I do not wish to attempt to explain. It is, however, I believe, reasonable to suppose that the toxins secreted by the bacilli in the lungs of a tuberculous mother and the general debility caused by them, impair often quite seriously the development of the child *in utero*.

As to the frequency of tuberculosis in childhood I will not burden this little address with many statistics. Permit me only to quote a few of the more interesting ones. Bollinger⁷ in 500 autopsies of children of all ages up to the fifteenth year found lesions of tuberculosis in 218 cases. In 150 of these the lesions were active and in 68 latent.

As to the time when children manifest the symptoms of tuberculosis most frequently, Heubner's⁸ statistics are instructive. Of 844 infants of which none suffered from tuberculosis at the time of their reception in the hospital, the development of the disease took place in 3.6% at the age of 3 to 6 months, in 11.8% at the age of 9 months, in 26.6% at the age of one year.

Of 458 children 14.2 % were found tuberculous at the age of 2 years.									
" 376	"	13.4	"	"	"	"	"	3	"
" 306	"	11.1	"	"	"	"	"	4	"
" 470	"	7.4	"	"	"	"	"	5-6	"
" 682	"	5.0	"	"	"	"	"	7-10	"

Let us incidentally remark that even these statistics seem to prove that children are very rarely born tuberculous. We know from animal experiments that the grosser pathological changes, brought about by the bacillus of tuberculosis, such as enlargement of the glands, are not produced before two or three months after the penetration of this micro-organism into the system.

According to Küss⁹ the maximum death rate from tuberculous lesions in childhood is reached between the second and fourth years. As to the *modus operandi* of the infection of children we have, of course, no statistics. To ascribe the very frequent intestinal tuberculosis found in childhood exclusively to a tuberculous milk supply would be unscientific. There is no doubt that many a child has been rendered tuberculous because of taking food coming from tuberculous cows, but in as many, perhaps even in more cases, intestinal tuberculosis is secondary and has resulted from the ingestion of pulmonary secretions, since small children never expectorate. Autopsies seem to show that a very large percentage of children have contracted tuberculosis by inhalation since the bronchial glands harbor the oldest foci and seem thus to represent the point of entry of the tuberculosis bacilli. The presence of bronchial and pulmonary foci and tuberculosis of the mesentery glands, when all lesions seem to be of the same duration, may well be explained by a double infection of the respiratory and alimentary tract of the child.

A more recent explanation of the frequent presence of tuberculosis in the bronchial glands as being also probably due to the ingestion of tuberculous milk, is given by Latham.¹⁰ According to this author the bacilli pass from the intestinal mucous membrane, by way of the lymphatics, to the bronchial glands. From these glands the process spreads to the lung tissue, 1, by direct continuity; 2, by means of the lymphatics but against the supposed lymphatic stream; 3, by ulcerating into a blood-vessel and in this way disseminating the bacilli all over the body; and 4, by ulcerating into a bronchus. The right set of glands is more commonly affected than the left. Latham, whose observations cover more than 3000 cases, admits, however, a very frequently infected air supply as a cause of tuberculosis in childhood. Thus we see that in young as well as in old, tuberculous infection can take place in three ways, namely, Inhalation, Ingestion and Inoculation.

The presence of a consumptive who is careless with his expectoration is sufficient to endanger the life of a child; and it is not at all necessary that the child should come in close contact with this individual. Heubner speaks of num-

⁴ Straus, "La tuberculose et son bacille."

⁵ Zeitschrift f. klin. Medizin, Bd. viii, 1884.

⁶ Annales des med. exp., vol. i, 1889.

⁷ D'Espine, Annales de med. et de chir. infantile; September 1, 1900.

⁸ "Zur Verhütung der Tuberkulose im Kindesalter," Congress of Tuberculosis, Berlin, 1899.

⁹ Küss, "De l'Hérédité parasitaire de la tuberculose humaine," Paris, 1898.

¹⁰ Latham, "Pulmonary Tuberculosis in Early Childhood," Lancet, December 22, 1900.

crous cases where children from healthy parents given into a family to board became tuberculous owing to the presence of a consumptive in that family.

The sputum coming from a tuberculous mother, father, relative or friend is a very frequent cause of the infection of little infants. Here the infectious germs may be ingested by the child with its saliva, but being kissed by tuberculous individuals is not the only source of the ingestion of tuberculous saliva. Midwives and sometimes also physicians will in the presence of an asphyxiated newborn child apply their mouth to that of the infant and inflate the child's chest to bring its respiratory organs into play. If the operator is consumptive the danger of imparting his or her disease to the infant is evident. In my recent book on tuberculosis¹¹ I quoted the remarkable case of Reich, which, I believe, will bear repeating here as an illustration: A midwife in the village of Neuenberg became consumptive in 1874, and died of this disease in July, 1876. Ten children, without hereditary predisposition, attended by this midwife between April, 1875, and May, 1876, died before reaching the age of seventeen months. This consumptive midwife was in the habit of sucking the mucus from the mouths of newborn children, and blowing air into their mouths when there was the slightest sign of asphyxia.

I was assured by a tuberculous mother that since the family physician had warned her never to kiss the child on the mouth, she had religiously refrained from doing so; but while telling me of this devotion I saw her tasting the food she was preparing for the child, to judge of its palatability and temperature, from the same spoon with which she fed her infant. In like manner the rubber nipple of the milk bottle may also become a source of infection.

Inoculation during early infancy is relatively rare, if we leave aside the comparatively numerous cases of tuberculous infection through ritual circumcision. I have been able to collect about twenty authentic cases, but the surgical literature of all countries where Israelites practice this rite in the orthodox way, continues to contain reports now and then of cases of tuberculous infection through this mode of circumcision. The tuberculous inoculation following this operation manifests itself first as a local disease of the genital organs from whence it becomes generalized in a great number of cases. The operation of circumcision, when skillfully and carefully performed, is in itself trifling, but the sucking of the prepuce afterwards makes it dangerous, for it is evident that if the operating rabbi should be a consumptive, inoculation is made very possible.

So much for the dangers to which the infant is exposed. When the child becomes old enough to creep about and play on the floor it is exposed to all three methods of infection at once. If there is a consumptive in the family and he is careless, ignorant or helpless, there will be ample opportunity

for the little one playing on the floor to inhale the dust laden with bacilli, coming from the pulverized and dried expectoration. Like all children it will touch everything on or near the floor and then put the fingers into the mouth. To conceive of a more certain method of ingesting tuberculosis is hardly possible. If the child's nails are not clean and closely cut it will inoculate itself with tuberculous substances. This method of infection happens quite often, particularly when the child is suffering from eczematous or other skin troubles. The result may be a local tuberculosis, or, perhaps, more frequently a lymphatic infection. To relieve the itching sensation produced by the irritating nasal secretions of a coryza, the child will poke its fingers into its nose and we may have there the starting point of a facial lupus. Older children are exposed to the same causes of infection, though perhaps in a lesser degree, when playing in public or private playgrounds, kindergartens, etc. That the infection of a child attending school from other tuberculous children of the same class, or even from a consumptive teacher, is possible, we must admit, especially in schools where the hygienic conditions are poor and where no sanitary supervision exists.

What remedies have we to suggest to counteract these multiple dangers to which children are exposed from the ever present bacillus tuberculosis?

To assure a rigorous prophylaxis against tuberculosis from the very earliest day of childhood I do not know of any better plan than to have printed directions issued by the boards of health, which should be in the hands of every physician and midwife to give to the future mother, to the nurse or the immediate members of the family. These instructions should contain everything relating to prophylaxis, general cleanliness, ventilation, nutrition, etc. The leaflets should be printed in plain, comprehensible language.

While it is now the almost universal practice never to let a child be nursed by a tuberculous mother, for the sake of preserving the strength and the life of the mother, prohibiting the tuberculous mother to become the nurse should also find a reason in the interest of the child. A tuberculous mother may transmit tuberculosis to the child through her milk.

While separating a child from the tuberculous mother and giving it the best hygienic and sanitary environments elsewhere, would be the ideal way of solving the problem, it is but rarely practicable. We must find means to protect a child in its own home. To avoid the inhalation of tuberculosis the greatest care should be exercised on the part of parents, relatives or friends with whom the child lives. The well-known precautions concerning the tuberculous expectoration, and also drop infection, that is to say, the ejection of small particles of bacilliferous saliva during the so-called dry cough, loud talking or sneezing, should be rigorously adhered to by everyone who may come in contact with the child. The child should not sleep with a tuberculous mother. It should have its own little bed from the day of its birth. The child should never be taken on visits to consumptive friends or relatives.

¹¹ Knopf, "Pulmonary Tuberculosis: Its Modern Prophylaxis and the Treatment in Special Institutions and at Home". P. Blakiston's Son & Co., Philadelphia, 1899.

As a matter of course, if a child should be removed from the parents' home and be boarded elsewhere, one should be sure that there is no consumptive in the new home of the infant, and that it is not frequented by consumptives. Day nurseries or infants' shelters where working women often leave their infants should be subject to thorough sanitary supervision and no tuberculous individual should be employed in such an establishment. In choosing a wetnurse or simple attendant to a child one should always assure oneself of the absolute health of the individual.

To combat the danger from ingestion of tuberculous cow's milk is, of course, primarily a duty which devolves upon sanitary authorities, the State, county, or city boards of health respectively. It is the duty of these authorities to make the sale of tuberculous milk practicably impossible. But to all mothers who do not nurse their children it should become a religious duty to boil or sterilize the child's milk, particularly in cities where one is never certain of the absolute purity of that article. Whenever it is possible cow's milk should be replaced by goat's milk, which, as is well known, is almost never tuberculous. When the child grows older and eats meat, all that is of doubtful origin should, of course, be thoroughly cooked.

To kiss the child on the mouth should not be allowed in any case, and as the child grows older it should be taught not to kiss strangers at all and relatives and friends only on the cheek. Caressing and kissing domestic pets, such as parrots, canary birds, dogs, cats, etc., should be discouraged.

Since we have spoken of the possibility of midwives or physicians infecting the newborn child in the attempt to bring its respiratory organs into play, we will also suggest a remedy. To avoid such accidents the mouth-to-mouth respiration should be replaced by the safer method of using the catheter, as recommended by Tarnier and Lusk. Laborde's method of rhythmical traction of the tongue will also suffice to cause the child to breathe if the obstructing mucus has been removed. A simple swab suffices to remove this mucus, and to do this by mouth-to-mouth suction is to be condemned.

The bottle and nipple through which the child receives its milk should be kept scrupulously clean, and the tuberculous mother should never put the nipple into her mouth. Later on, when the infant is old enough to be fed with a spoon she should again bear in mind that her own saliva is likely to be bacilliferous and she should avoid using the same spoon for herself and child. The remnants of food left by a tuberculous invalid should not be eaten by any one, but more particularly not by a child, neither should the latter eat any food handled by a consumptive.

Inoculation of tuberculosis of an infant through the orthodox rite of circumcision will be difficult to combat by a simple protest against this operation on the part of physicians, although it is well known that syphilis and diphtheria have also been transmitted through this suction process, and that through lack of skill in after treatment, secondary hemorrhage, erysipelas and gangrene having ensued, orthodox

Hebrews will rarely permit any modification in this procedure. I would therefore suggest as a remedy that only such persons should be allowed to perform circumcision as have shown the necessary skill before a medical board of examiners, and that every time they are called upon to perform the rite they should submit themselves to a medical examination. Only when bearing a certificate from a regular physician, stating the absolute freedom from specific diseases, should they be allowed to perform ritual circumcision.

As another reliable prophylactic measure against the possibility of inoculating the child when the parents insist upon the orthodox method of circumcision, is the suction by the aid of a glass tube, as practiced in France and Germany.

So much for the measures to protect the infant during his earliest age from the possibility of infection in the three ways, inhalation, ingestion, and inoculation. We will now see what can be done in the line of prophylaxis for the child who creeps on the floor, learns to walk, visits kindergartens, plays on public or private playgrounds, visits menageries, and finally goes to school.

The floor of the rooms where the child lives and on which it plays should not be carpeted. It should be kept scrupulously clean and, if desired, a clean mat may replace the carpet. To keep the ordinary wooden floor clean and as far as possible aseptic, the use of petroleum wax as recommended by R. Petit¹² should be endorsed. Experiments have demonstrated that the various pathogenic microbes, such as the bacillus of diphtheria, of typhoid fever, the streptococci and staphylococci, and the bacterium coli, can not live in this substance, and the tubercle bacillus loses its virulence when in contact with it. The cracks in the floors should be filled and also covered with this substance. Water and even antiseptic substances do not alter this wax. The ordinary broom should never be used in cleaning children's rooms; if wiping the floor is not practicable it should be swept with moistened sawdust. All these precautions recommended for the children's rooms in the private home should, of course, be practiced if possible even with more rigor in public nurseries, kindergartens, asylums, orphanages, etc.

In view of the possibility of infecting any room by drop infection it is best that the consumptive, even if ordinarily careful with his expectoration, should sojourn as little as possible in the children's rooms. Of course, it goes without saying that neither spitting nor smoking should be allowed in children's quarters. Expectoration on or near public or private playgrounds should be considered a misdemeanor and punished accordingly. These grounds should be kept specially clean and from time to time be strewn with clean gravel.

The greatly loved visits of little ones to menageries must be of concern to the sanitarian who desires to protect the children from tuberculosis. To visit the ape house in the zoological gardens and to remain there as long as possible is

¹² "Récherches sur un procédé simple pour aseptiser les planchers," Congrès de la Tuberculose, 1898.

the delight of children, and yet, perhaps next to cattle there are no animals so subject to tuberculosis as apes. Add to this the commotion, dust, and impure air in the average ape-house at the usual time of the children's visits, and one cannot help thinking of an absolute danger. The managers of menageries and zoological gardens should do their very best to reduce this source of infection to the least possible minimum. A tuberculous keeper might very easily infect the animals under his care, especially since their confinement makes them particularly susceptible to the invasion of the bacilli. The law which authorizes the killing of tuberculous cattle should be extended to all other animals as well. There seems no reason why an ape house, containing numerous con-

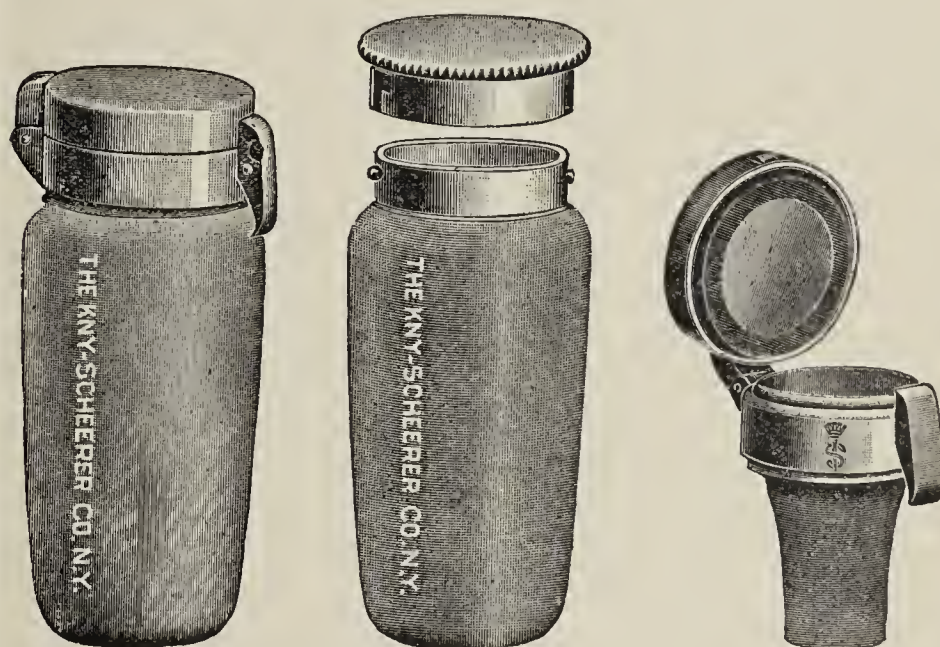


sumptive animals, should not be as much a source of infection as a tenement house where ignorant or careless tuberculous individuals have expectorated indiscriminately. Expectorating on the floor or anywhere else in these menageries should be strictly prohibited to keepers as well as to visitors, and the floor should always be strewn with moistened sawdust during visiting hours.

The hygiene which should prevail in the kindergarten and playroom should, of course, also be universal in the school-house. School children should be taught the use of spittoons and handkerchiefs. Expectorating anywhere except in a proper receptacle should be punished in the same way as any violation of class rules. The elevated non-breakable spittoon should be given preference to the ordinary porcelain or glass cuspidor placed on the floor. I have often wondered if the individual pocket flask in the public school would not also tend to decrease epidemics of hiccoughs,

measles, and grippe, besides being one of the best means of preventing the contraction of tuberculosis through indiscriminate expectoration. Each child should have a cupboard where he should keep his own towel and drinking-cup. To avoid drop infection, children should be taught to always hold a handkerchief before their mouth while coughing or sneezing.

Obligatory periodical disinfection of the schoolroom by formaldehyde gas may also be advantageously instituted. To make the disinfecting and cleansing of the classroom as thorough as possible, I would suggest that desks and chairs be so constructed that they can easily be folded together after school hours. This innovation in school hygiene was first inaugurated by School Superintendent Akbroit, of Odessa, with most satisfactory results. As another sanitary measure I would insist that lady school teachers and the grown-up girl pupils should not under penalty of discharge, be allowed to wear trailing dresses. The short rainy-day skirt is, in my humble opinion, most becoming to teachers and pupils, and certainly far more sanitary than the trailing skirt which so often is made to do the scavenger's dirty work.



The fundamental principles of hygiene, especially in regard to the prevention of tuberculosis, should be made part of the curriculum in every class. I was told by Dr. Roger S. Tracy, of the New York Board of Health, that there existed in some town out west, the name of which he had forgotten, the custom of inclosing a leaflet for the teaching of hygiene in every book belonging to the school. Now, it seems to me that this is an excellent idea and a good way to teach the fundamental principles of general hygiene and particularly the prevention of tuberculosis, and I would strongly recommend this plan to all our boards of education.

Kissing, which is such a prevalent practice in some girls' schools, should be discouraged and designated as unhygienic. While children suffering simply from scrofulous manifestations might be permitted in public schools, all pupils suffering from pulmonary tuberculosis, or teachers afflicted with the same disease should not be allowed there.

The early recognition of pulmonary tuberculosis, which is so essential in the solution of the tuberculosis problem in the adult, is equally important in regard to the combat of this disease in childhood. Here comes a function of the school physician (and no school should be without one) which, I believe, has not as yet been sufficiently appreciated nor exercised. The chest of every child attending the public school and every teacher teaching there should be carefully examined at least twice or three times a year, if owing to a large number of pupils this can not be done every three months. Through the early discovery of tuberculosis in a pupil, an immediate warning to the parents, and timely and judicious treatment many a young life will be saved.

To prevent an inoculation tuberculosis during the time the child is likely to play on the floor, mothers and nurses should see that the child's fingers are kept as clean as possible and his nails cut. As long as the child is too small to clean its nose, regular nasal toilets with some mild borated solution or warm previously boiled water should be instituted. Eczemas and other skin eruptions should receive immediate medical attention, for, as has been said, left to themselves they may give entrance to tuberculous infection.

We come now to the second portion of our discourse, which treats of the hereditary disposition which the child of tuberculous parentage possesses at birth. We may define this hereditary disposition in two ways. As bacteriologists we would probably say a hereditary predisposition is that peculiar condition whereby the various organs, and in particular the respiratory and next to it the intestinal tract, offer a very favorable soil or culture medium for the development and multiplication of the bacilli. As clinicians we might say hereditary predisposition to tuberculosis means a physiological poverty, brought as an inheritance into this world, whereby the system is minus phagocytic and bactericidal powers inherent in strong and healthy organisms.

It is well known that the transmission of a tuberculous tendency comes most frequently from the maternal side. The most radical means of preventing a progeny subject to tuberculosis would, of course, be the interdiction of marriage to all tuberculous individuals. Our present state of society and our conception of individual liberty will scarcely make it possible for the time being, to inaugurate legislative means to counteract marriages between tuberculous individuals. General education and enlightenment on this question may be helpful as a prophylactic means, but the family physician will have to do the bulk of the work in preventing such dangerous unions. Even the cured consumptive should not think of marrying until a considerable time after his complete restoration to health. Gerhardt¹³ counsels to wait at least one year, but I consider this hardly enough and would much rather make it two years.

To bring about abortion when a conception has taken place in a tuberculous mother I consider useless. Instead of

saving one life there is the danger of sacrificing two; but in view of our present knowledge of tuberculosis I have no hesitation to declare that I do not consider it a sin either before God or man to instruct a tuberculous mother or father that they may not procreate a tuberculous issue. If, in spite of the warning of the family physician, a tuberculous mother has conceived, what are we to do? Shall we leave the mother and child to their fate? Surely not! Though the mother may be suffering from tuberculosis and the child seemingly be doomed to become a candidate for consumption, modern therapy has taught us not to despair, and we may save the lives of both; but we must begin by treating the child *in utero* and with this, of course, begin a thorough treatment of the mother's condition, and continue it at least a year after confinement. A woman who is to give birth to a child should abandon the corset and tight clothing in time to allow a continued, free abdominal and thoracic respiration. Better yet is it if she has never been addicted to the habit of tight lacing, for the experiments of Kellogg¹⁴ and Mays have demonstrated that the so-called female or costal type of respiration which prevails among civilized women is the result of their restricting and unhygienic mode of dress, and is not due to the influence of gestation or to a natural difference in the anatomy and physiological growth of man and woman. If a support for an unusually large breast must be worn let the corset be replaced by a comfortable waist which permits free and deep respiratory movements. Instead of tying her skirts around the waist she should wear them suspended from the shoulders. By wearing a close-fitting union-suit for underwear of wool or cotton, according to the season, it will be possible to get along with less skirts and thus lessen the weight around the waist. In short, the whole dress of the mother should be so arranged that there are no restrictions and that no organ in the body should be hindered in its free physiological functions. For the future mother to live as much as possible in pure, fresh air, to take frequent breathing exercises, to avoid crowded assemblies where the air is vitiated, to live, in short, as hygienic a life as the family's social condition will permit, will have a most salutary effect on the child's health. If the circumstances are such that you can induce this family with a tuberculous mother, living in the city, to move to the country or to a smaller town where modern hygienic conveniences can be had, but where the crowded and noisy conditions of city life are absent, so much the better for the prospects of mother and child.

The newborn babe is in need of pure, fresh air as much as the mother; and the lying-in room and the nursery should always be well ventilated. When in due time the child is taken for an airing, the thick, almost impermeable veil should be abandoned. These veils, often tightened around the little face, press against the nose and make it difficult for the

¹³ "Ueber Eheschliessungen Tuberkulöser," Zeitschr. f. Tuberkulose u. Heilstättenwesen, September, 1900.

¹⁴ Kellogg, "Experimental Researches Respecting the Relation of Dress to Pelvic Diseases of Women", Transactions of the Michigan State Medical Society, 1888.

child to breathe naturally, yet the mother wonders how the baby got into the habit of breathing through the mouth.

Frequently also, mouth-breathing in children, and sometimes in adults, must be attributed to adenoid vegetation in the nasopharynx, or to enlarged tonsils. These as well as all other causes of obstruction to a free, natural respiration, such as deviated septum, enlarged turbinated bones, hypertrophied mucous membrane, polypi, etc., must be removed if we desire to protect the child or adult from chronic nasal, pharyngeal, or laryngeal catarrhs, so often the forerunners of pulmonary disease.

The proper bringing up of children that have a tendency to become tuberculous is of the greatest importance. Many are poor eaters from the day of their birth. Discipline, not to allow too many sweets, to observe regular meal-times, and to keep the bowels in good condition, are the best means to combat a dislike for eating. As early as possible children should be taught to clean their teeth thoroughly after each meal, for a good digestion is dependent upon the good state of the teeth. The dislike to play outdoors, which is so characteristic of the little candidates for tuberculous diseases, can also only be overcome by discipline. To dress them too warmly and bundle them up all the time is as injurious as having them remain most of the time indoors. This hardening of the constitution will be the best method to counteract a disposition to take cold easily, which in children predisposed to tuberculosis has often a tendency to develop catarrhs of the deeper respiratory tract.

I consider the air-bath and sun-bath for children at the earliest age most beneficial. Let the little ones toddle around naked every day for a short time; in cold weather in well-warmed rooms, and in summer in a room bathed by the rays of the sun, but always on a clean floor or clean Japanese matting. With their growing intelligence children should be taught by practice and example the value and the love of pure, fresh air. As soon as the age and intelligence of the child will permit, breathing exercises should be taught him. He should learn to like them as the average child does general gymnastics.

The lying-in room, the nurseries and playrooms must always be well ventilated. Public as well as private schools and colleges should be model houses in regard to cleanliness, hygiene and constant ventilation. Ventilation not only when the children have left, but all the time, and, as Emmert¹⁵ says, since windows and doors alone do not suffice to properly ventilate rooms when occupied by a mass of human beings, mechanical devices should be resorted to to secure always a plentiful supply of fresh air. Overwork during school life is an indirect cause of furthering a tuberculous tendency in many children, and indeed it is injurious even to a healthy child. Much out-door play, singing and reciting in the open air should be encouraged. This life out of doors, the love for pure and fresh air, for gymnastics and out-door sports should

be kept up by the young man and girl leaving school throughout life.

In choosing his future career the young man born with that peculiar susceptibility which Peter describes so aptly as "*tuberculisable*" should seek professions which will demand out-door life. Farming, gardening and forestry will assure him the longest and most useful existence.

Hydrotherapeutics, as a measure to prevent pulmonary tuberculosis, tends to develop to more vigorous action the vasomotor system; it also should be instituted at an early age. A child, a few months old, can support with impunity a rapid sponging off with cold water after its warm bath, followed by a relatively vigorous friction with a soft Turkish towel. As the child grows older he should not only be taught this use of cold water after his semi-weekly or weekly warm bath, but he should wash at least the face, neck and chest every morning with cold water. Better yet, if he can accustom himself early to a daily cold douche. The utility of all-the-year-round swimming baths, where old and young of all classes can, gratuitously or for a moderate price, enjoy the salutary effects on body and mind of a good swim, is too well known to need to be insisted on.

There should be many small parks and playgrounds and public baths for old and young in the densely crowded districts of our large cities. City parks have justly been called the lungs of great centers of population. Here mothers and children of the poor can breathe purer and fresher air, which is one of the best means of preventing tuberculosis.

I have thus far but slightly touched on the sociological side of prophylaxis. I have not made much distinction between scrofulous and tuberculous diseases, for the former is but a lighter form of tuberculosis. The same sociological conditions which further tuberculosis in the pulmonary form further also scrofulous diseases. Children from syphilitic and alcoholic parents are particularly prone to tuberculous and scrofulous affections. In seeking to prevent tuberculous and scrofulous diseases in childhood we must combat our two great social evils, syphilis and alcoholism.

Here I cannot help also denouncing strongly the employment of children under fourteen years of age in various industries requiring often six to ten hours of continued manual labor, and often in factories and mines where work even taxes the healthy organs of a full-grown man.

Of the frequency of scrofulous and tuberculous troubles among children of the poor one has scarcely an idea. In one of the public schools of Berlin, where careful statistics are kept concerning the daily attendance of the children, it was found that out of 125 boys and 132 girls who did not attend school regularly, not less than 112 of the former and 115 of the latter suffered from tuberculous or scrofulous troubles. As to what is best to do for the underfed pupils, the children of poor parents, attending our public schools, I would suggest a philanthropic enterprise which would cost little and which would do a world of good. Provide them with a lunch of a few good meat sandwiches and one or two glasses of good milk, and I am convinced that fewer

¹⁵ Emmert, "Is Our Public School System Conducive to Tuberculosis?" Transactions of the Iowa State Med. Society, 1898.

will develop tuberculosis and scrofulosis, and they will do better work at school and at home. A similar experiment has been tried recently in one of the German schools for the poor, and the results have been most gratifying; nearly everyone of the children gained in weight and strength in a relatively short time.

For children suffering from either tuberculous or scrofulous manifestations the treatment is well known. Codliver oil, arsenic, iron, but above all hygienic and dietetic measures, aero-, hydro- and solar therapy, under constant medical supervision in a good healthy locality, preferably in sanatoria erected for that purpose in the country or on the seashore, have proven to be the most efficacious means to treat these diseases during childhood. With so many beautiful places in our inland and seacoast towns, which would be suitable for children's sanatoria, it is to be regretted that we have almost no such institutions as yet. In France, Germany, Holland and Italy there exist numerous children's sanatoria for the treatment of tuberculous and scrofulous diseases. To these are attached splendid schools so that the intellectual side of the children's training is not neglected. The results obtained in these institutions for the little sufferers are even better than those for adults, the latest reports giving as much as 50 to 75% of complete cures.

Under medical news from Colorado I read in last week's Journal of the American Medical Association (May 18th), that by order of State Health Commissioner Clough, promulgated April 15th, sufferers from tuberculosis are excluded from public schools. This means, of course, an exclusion of tuberculous pupils and teachers alike. But, I ask, has

the State of Colorado provided another place of instruction for these little ones? Is it just to exclude a child from public school for so long a time as the cure of such a chronic disease as tuberculosis must of necessity require? The action of any health authority in suppressing tuberculosis in public schools should be commended, but before enforcing the regulations which deprive the child of the right and privilege of education, those authorities should see that specially constructed sanatoria-schools should be erected where these little ones receive not only the benefit of judicious medical treatment and practical hygienic training, but also that school education to which every American child is entitled.

There is a strong awakening now for the need of sanatoria for consumptive adults throughout the United States. Let us in our eagerness to treat the consumptive man and woman not forget that to treat tuberculous and scrofulous children is just as important. These special children's sanatoria, situated on the seacoast or inland in particularly healthy localities, are powerful agents in the prevention and cure of tuberculosis. By carrying out the prophylactic measures which I endeavored to outline in the first portion of my lecture and by providing institutions for children already afflicted with tuberculous or scrofulous diseases, we will prevent many a one from becoming a consumptive man or woman. Through prevention and timely cure these little ones have many chances to become strong, healthy and useful members of the community. Let us take good care of the little children and never forget that the child of to-day will be the man of to-morrow.

16 West Ninety-Fifth Street.

RESPIRATORY EXERCISES IN THE PREVENTION AND TREATMENT OF PULMONARY DISEASES.¹

BY S. A. KNOPP, M. D., New York City.

I have chosen this subject for the second lecture which I have the honor to deliver before you, in the hope that it may result in some practical good, not only to your patients, but also to yourselves. We as physicians are very apt to neglect our own health. Often deeply absorbed in our work we forget, for example, to take our meals regularly; or we eat hastily, and do not rest when we ought to rest. The general practitioner, and the majority of us are general practitioners, is the greatest sinner in this respect. We will often scold the members of the families, whose physicians we may be, if we discover them to be neglectful in these matters so essential to a healthful life, and still every day we are doing the very things which we tell them not to do.

I believe this is a good opportunity to sound a note of warning. I have the honor of addressing physicians older

than myself, some of my age, and some a good deal younger. Of the older ones I must ask pardon for trying to teach them what they know better than I, but what I know they only teach to others and rarely practice themselves. These, my seniors, I will only remind what a good thing it would be for their own welfare to practice as regularly as possible what they preach so frequently. To my colleagues and younger friends I will say, preach regular living to your patients and practice it yourselves. As a rule take your meals regularly, irregularly only as an exception. Take time for your meals and only eat hastily when it must be done. Never start out to work with an empty stomach. Get eight to nine hours sleep out of every twenty-four; if not possible to have it in one stretch, take this time, necessary for recuperation, in installments. Eight hours of sleep, regular meals, good nutrition, good digestion, and proper assimilation of our food are, however, not more important to our well-being and that of our patients than good air and proper

¹ Lecture delivered before the Senior and Post-graduate Classes of Johns Hopkins Medical School, May 29, 1901.

breathing. The natural man breathes physiologically; but civilization with the many blessings it has conferred upon us has also brought to us certain customs in the shape of dress, habitation, and occupation, which interfere with the natural process of breathing, on one hand by restricting our thoracic and abdominal organs by uncomfortable dress or peculiar posture, and on the other by placing us in environments which make it impossible for us to get constantly a sufficient amount of fresh, pure air.

Let us first try to define what natural breathing is. While air may enter the respiratory tract of man through the mouth when he is speaking, for the greater part of his existence he should breathe through the nose. The nose is the natural organ for the entrance of air. Its osseous conformation and its lining, the Schneiderian membrane, have the function to protect the deeper respiratory tract from foreign and irritating substances, and to render the cold air inspired warm enough not to be injurious to the delicate pulmonary structure. The first requisite then for good natural breathing is a nose free from all obstructions. Spurs, a deviated septum, polypi, or a marked hypertrophy of the mucous membrane, adenoid vegetations, in short, whatever prevent the air from passing freely through the upper respiratory tract, are a hindrance to the natural respiratory process. Only by removing these hindrances can we hope to get the benefit of a natural respiration.

Of the value of right physiological breathing in the prevention of disease, it is not necessary to dwell at length before an audience of physicians and advanced students in medicine, but I hope that I may not hurt the feelings of anybody in this amphitheater when I say that in order to impress upon your patient the importance of natural physiological breathing you must practice it yourselves. My main object to-night is to show the value of special breathing exercises in the development of the child, in the prevention of pulmonary diseases, particularly of consumption, and to describe and demonstrate some exercises which seem to me particularly useful in phthisiotherapy and the treatment of some other pulmonary affections.

After having assured yourselves that there is no obstruction in the upper respiratory tract to the free entrance of air, the next most important step is to see that the clothing of the individual to whom you intend to teach breathing exercises, whether he be man, woman or child, does not constrict either throat, thorax or abdomen. The man or woman with a high or tight collar or other neckwear constricting the throat, cannot possibly breathe deeply nor correctly. Not only women but men also at times have the clothing too tight around the chest to permit a free expansion of the thorax. Some men think they can breathe better by wearing belts to hold their trousers. I do not approve of wearing belts for that purpose; it does not facilitate breathing and interferes with the peristaltic action of the intestines, and it may even be the cause of the development of a hernia. While the man perhaps will acknowledge that he is uncomfortably dressed when you so tell him or that the belt, if he wears

one, is too tight, a woman will but rarely do so. If she wears a corset she will assure you that it is not at all tightly laced and that there are really no constricting bands around her waist. You must exert all possible tact to convince her of this error, for I believe I do not exaggerate when I say that a large majority of women wearing corsets wear them altogether too tight. Some women must wear a support of some kind, but many of them could get along very well without one, and none need a tightly laced corset, nor need they fasten their skirts in such a way as to constrict the abdomen. If they only would develop their thoracic muscles they would have a natural and more graceful carriage than the one obtained by that little instrument of torture, called the corset. Whenever a support is indispensable let women wear a corset-waist without steel-bones. Skirts should be worn in such a manner that the weight is carried by the shoulders.

A good way to convince your pupil or patient that uncomfortable and restricting garments do not permit free expansion of the chest is as follows: Tell him or her to stand in the morning before dressing and in the evening before retiring, stripped to the waist, in front of the looking glass and there take the breathing exercises which we will describe presently. The pupils or patients will thus realize the difference between breathing with or without restricting garments. They will watch their respiratory muscles developing, and become intensely interested in these lung gymnastics. The exposure of the chest to the air for a few minutes every morning and evening has an additional advantage. The skin which is also a respiratory organ receives a healthful stimulation through this exposure to the cool air. I venture even to say that this air-bath of throat and chest, when regularly practiced, will have a most beneficent influence in the prevention of colds.

Presuming then that you have satisfied yourselves that the pupil to whom you are to teach respiratory exercises is dressed in such a manner that there remains not the slightest restriction around throat, thorax or abdomen, you can begin your instructions. It goes, of course, without saying, that you should teach the breathing exercises always either in the open air or in a well ventilated room, preferably in front of an open window. A locality where the individual, by taking deep breaths, would only inhale an additional amount of impure odors or dust, is, of course, not suitable as a place for teaching breathing exercises. Starting out with the presumption that we find ourselves in suitable environment for respiratory gymnastics we teach our pupil to assume the position of the military "attention"—heels together, body erect, chest forward, head straight, the palms of the hands touching the external portion of the thigh. We tell the pupil to keep his mouth closed and to take a slow deep inspiration through the nose, that is to say, taking in all the air possible with one inspiratory movement, to hold his breath a few seconds, and then exhale just a trifle faster. If the pupil has done this act well, we supplement it by allowing him to raise the arms to a horizontal position. He does this during the act of inspiration, remains in that position for a few seconds

and while exhaling brings the arms down to the original position. The act of expiration should again be a little more rapid than that of inspiration.

When the first exercise (Fig. 1) is thoroughly mastered after a few days, the pupil can be taught a second one, which is like the first except that the upward movement of the arms is continued until the hands meet over the head (Fig. 1). The third respiratory exercise, somewhat more difficult and requiring more strength and endurance, should not be undertaken until the first two have been mastered and practiced for several days. The third exercise might justly be called a dry swim; one takes the same military position of "attention," heels together, body erect, and then stretches out the arms as in the act of swimming, the dorsal surfaces

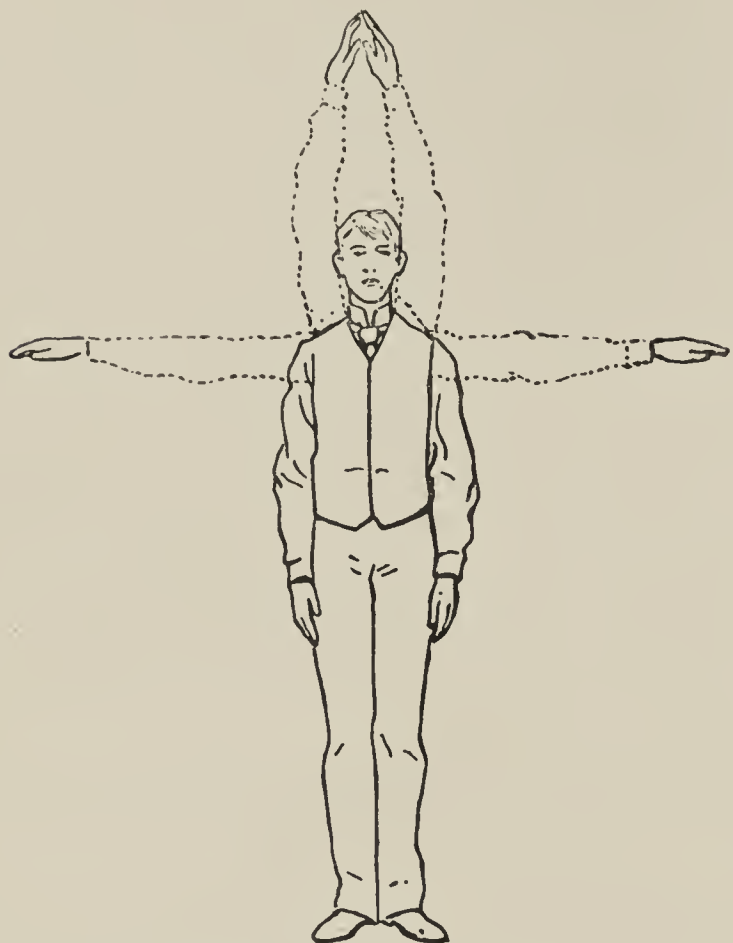


FIG. 1.—First and Second Breathing Exercises.

of the hands touching each other. He then moves the arms, just as if he was dividing the water, during the act of inspiration, the hands meeting finally behind the back. The pupil remains in this position for a few seconds, retains the air, and during exhalation brings the arms forward. This somewhat difficult exercise can be facilitated and made more effective by rising on the toes during the act of inspiration and descending during the act of expiration (Fig. 2.)

Valuable as these exercises with the moving of the arms are, they cannot be practiced everywhere and at all times without attracting attention. Under such conditions one must often content oneself with raising the shoulders, making a rotary movement backward during the act of inhalation, remain in this position, holding the breath for a few seconds and then exhale while moving the shoulders forward and downward, assuming again the normal position. This

exercise (Fig. 3) can even be taken while walking and, of course, very easily while sitting or riding in the open air.

Young girls and boys, and especially those who are predisposed to consumption, often acquire a habit of stooping. To overcome this the following exercise is to be recommended. The child makes his best effort to stand straight, places his hands on his hips with the thumbs in front, and then bends slowly backward as far as he can during the act of inhaling. He remains in this position for a few seconds, while holding the breath, and then rises again somewhat more rapidly, during the act of exhalation (Fig. 4).

Concerning the general directions as to the frequency and order of these exercises I can only say here the same that I have said in previous writings when speaking of acrothera-



FIG. 2.—Third Breathing Exercise.

peutics proper: Commence always with the easier exercises and only gradually take the more difficult ones. Repeat the exercises from six to nine times either of one kind or the other, every half hour or so, or three of each, and continue this practice until deep breathing has become a natural habit. One rule which is applicable as well to the pupil whom you teach to breathe to prevent disease as to the patient for whom you prescribe respiratory exercises as a means of cure, is the following: Instruct them never to take the exercises when tired and never to continue them so long as to become tired.

Before we proceed to discuss the specific respiratory exercises suitable in diseases, let us also say a few words of the value of speaking, reciting and singing in the open air, or at least in well ventilated rooms or halls. To my mind there is not enough done in the physical education of our

children in this respect. Cases of phthisis which had even passed the incipient stage have been recorded as cured in individuals who, after realizing their condition, decided to follow the occupation of street singer or speaker. I know of the case of an English lady who became an evangelist addressing crowds of people every night in open air meetings and who actually was cured from her tuberculous disease after following this calling for a year. Barth, of Köslin, who has made a careful study of the effects of singing on the action of the lungs and heart, on diseases of the heart, on the pulmonary circulation, on the blood, the vocal apparatus, the upper air passages, the ear, the general health, the development of the chest, on metabolism, and on the activity of the digestive organs, has come to the conclusion that sing-

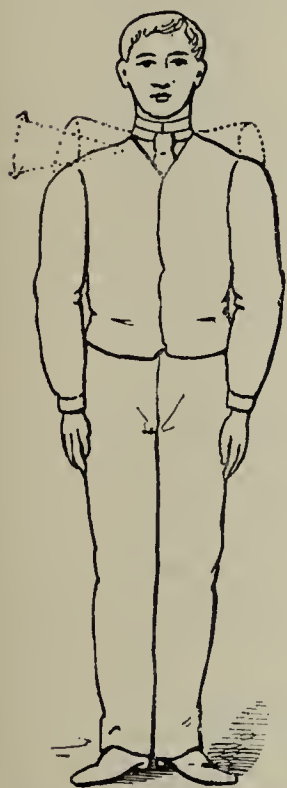


FIG. 3.—Breathing Exercise with Rolling of Shoulders.



FIG. 4.—Exercise for People in the Habit of Stooping.

ing is one of the exercises most conducive to health. Considering the fact that it can be practiced anywhere (when the air is pure) or at any time, without apparatus, it should be much more cultivated than it actually is. The German military authorities, who have the reputation of instituting all exercises which tend to invigorate the soldiers, have of late years encouraged singing by the troops during marches.

We will now speak of respiratory exercises in their therapeutical aspect in various pulmonary diseases. The six pathological conditions of the respiratory system which may be very greatly helped by proper judicious breathing exercises, are bronchitis, asthma, emphysema, an inactive lung owing to a badly resolved or slowly resolving pneumonia, deficient breathing owing to pleuritic adhesion, the remainder of an inflammation of the pleura, or convalescent emphysema, and last but not least, pulmonary tuberculosis.

In ordinary bronchitis, after the acute febrile state has passed, the exercises taught above for the development of a good breathing capacity in children, will answer for all practical purposes. These deep inspirations and expirations will be particularly useful in dissolving the mucus and making the expectoration easier. Except in simple bronchitis or badly resolved pneumonia you will probably find in the affections, just enumerated, if not a deficient development, a more or less pronounced atrophy or inactivity of the abdominal and thoracic muscles which should come into play in deep natural breathing. There is no use in teaching or prescribing respiratory exercises if the muscles which are to perform these exercises are lazy, badly developed or atrophied.

How are we to overcome such an atrophy in an emphysematous, asthmatic or phthisical patient? Electricity and massage are, of course, the best remedies. The most important of the two, and the one which I prefer, is certainly a proper, skillful and regular massage of the abdominal and thoracic muscles. While I do not expect every physician to massage his own cases, it seems to me equally unwise to leave the work entirely to the masseur, masseuse or nurse and content ourselves with telling these, our assistants, simply to massage the patient. We should certainly know ourselves how to do this massage and how to give instruction in this important physical method of curing disease.

Allow me to describe here and to demonstrate before you the method of massaging a patient with badly developed abdominal and thoracic muscles, which has given me the most satisfactory results. I place the patient on a moderately high table or bed with no springs. The height of the bed or table should be suited to the height of the operator. The latter must be able to bend comfortably over the patient and exert a moderate amount of force without getting too tired himself. A low bed with spring can not be used for applying scientific massage.

The room in which the patient is to be massaged should be comfortably warm and always well ventilated. To avoid unnecessary exposure it is well to have a shawl handy so as to protect that portion of the patient which is not manipulated at the time. Whether or not to use vaseline or some other substance for the purpose of lubrication will largely depend upon the masseur or patient. As a rule lubricants are not essential; of course there are cases of tuberculosis, and especially in children, where the use of codliver oil for this purpose may be very advisable.

The four movements which I employ are the following: friction, kneading, tapping and pinching. In the friction movement, and as much as possible in all the others, I like to follow the course of the venous circulation; in abdominal massage I like to bear in mind the situation of the colon, and thus at the same time aid in overcoming a tendency to constipation. This is done by massaging the colon separately, following its course along the ascending, transverse and descending portion. Around the umbilicus a circular motion from right to left is the best to be employed. This

massage of the abdominal wall should be more gentle than that of any other portion of the body and should be supplemented by teaching the patient to retract and relax his diaphragm alternately, holding it for several seconds in the retracted position so as to strengthen all the abdominal muscles. This exercise of diaphragm and abdominal muscles should be taught first to the patient in the recumbent position; later on he should learn to make this movement also in the standing posture. The massage which has the purpose of overcoming an atrophy of the respiratory muscles so that the act of respiration should be more complete, must not in the pulmonary invalid, and particularly in one suffering from chronic tuberculosis, be confined to abdomen and thorax alone, but must include the arms and shoulders as well.

Here is what I believe to be the most convenient method to massage the anterior muscles of forearms, arms, shoulders and thorax. Begin your friction at the tips of the fingers going as far as to the wrist articulation, from there to elbow joints, from elbow to shoulder. By a semi-circular movement, with moderately spread fingers and the palms of the hands, try to take in by your friction movement as much as possible of the posterior and lateral portion of the thorax.

After a few minutes of friction begin your true massage, that is to say, kneading, from the French *masser*, to knead. Manipulate the muscles so as to lift them from the osseous attachment and in the same order as the friction movement. The third movement is the tapping, which may be done with the whole hand, the palmar surface of the four fingers, or if desirable to avoid the clapping sound produced by this movement, tap with the ulnar surface of your hand, producing a sort of chopping movement.

The fourth movement I recommend is pinching, of which the particular purpose is to massage the skin. Pinch rapidly the various portions of the skin which you have already manipulated by friction, kneading and tapping. This pinching is most conveniently done, with least pain to the patient, by lifting a small portion of the skin between the thumb and the index and middle finger.

You now turn the patient on his chest with either the right or left cheek resting on a pillow so that he can breathe easily, while you manipulate the posterior muscles of arms, forearms, etc. in the same order as you did the anterior portion. If you are tall and vigorous and the patient not larger than you, it is possible to apply the friction movement to both arms, both shoulders and right and left portion of the thorax at the same time. This is done by placing the palms of your hands on the posterior portion of the patient's hands and then apply a good friction movement over hands, forearms, arms, shoulders and the posterior portion of the patient's thorax. The kneading, tapping and pinching movements are, of course, the same as for the anterior portion with the only difference that the posterior muscles of the trunk will stand a more vigorous massage than the anterior ones. The time occupied for anterior and posterior thoracic massage should be about thirty to forty minutes.

An exercise which the patient may be taught while in bed

and which will add to the good effect of the massage is the following: The patient lies on his back with a small pillow placed under him at about the height of the kidneys, so as to lift up the thorax. He then raises the arms in the air above his head so as to describe a half circle with them. He can, while raising the arms, take a deep inhalation, hold the breath for a moment, and return them to the original position during the act of exhalation, thus adding by active movement to the good effect of the massage. Should your patient be a child your ingenuity will probably be taxed at times in overcoming the thoracic malformation. You will have to resort to some special gymnastics, which, according to the indications, may even have to be aided by a special apparatus for exercising or by orthopedic appliances. The combination of all these means to correct a thoracic malformation is, however, most gratifying in these young children, and I am convinced that if more attention would be paid to the correction of those malformations which prevent the child's lungs from freely expanding, there would be fewer cases of tuberculosis in adult life.

Returning to our adult patient, and presuming that his more or less pronounced atrophy of the respiratory muscles has improved sufficiently under this massage, we will proceed to show what can be done in the various pathological conditions of the lungs through special and judicious respiratory exercise. Emphysema and asthma require a particular kind of respiratory exercise. While, as a general rule in respiratory therapeutics, the act of expiration should always be somewhat shorter than the act of inspiration, in these two diseases we must rather try to prolong the expiratory act. Having by our massage improved the thoracic muscles and the often very flabby condition of the abdominal walls of such an invalid, we tell him to bring all his respiratory muscles into play during the expiratory act. He inhales quietly through the nose as in ordinary inspiration, but we teach him to exhale with his mouth open and place the palms of his hands on his chest, the thumbs directly toward the axillary region, and then exert a strong pressure on his thorax. Through this exercise we endeavor to produce a long continued exhalation. Another valuable aid in recovering the lost tonicity of the pulmonary tissue through respiratory gymnastics is the following exercise which is particularly useful because it can be done without attracting attention, since the pressure with the hands on the thorax, while a valuable help is not always essential nor practical. The patient is told to inhale ordinarily, but during the act of exhaling to place his lips as if about to whistle and then produce a blowing sound as long as he can without taking another breath. We have him repeat this quite a number of times a day, but always according to our formula—never when he is tired and never to the extent of getting tired. The improvement in the condition of many asthmatic and emphysematous patients through such exercises is simply surprising, and while I, of course, would not wish to underestimate any other hygienic, dietetic or medicinal treatment in the various forms of asthma or emphysema, I do claim

that these exercises are most valuable adjuvants in the therapeutic management of such invalids.

We now come to such exercises as I would advise with judicious gradation in number and kind in conditions where either through a badly resolved pneumonia, old pleuritic adhesions, tuberculous deposits, or infiltration there is no longer a proper physiological breathing and sufficient hæmatosis. The exercises I am to describe I have, of course, most frequently employed with my tuberculous patients; but, valuable as they are, I wish to speak first to you of the contraindications, for respiratory exercises in pulmonary tuberculosis, or any other affection of the lungs, must not be blindly prescribed. A patient in a highly febrile state, or during an acute exacerbation of the tuberculous process, or an active hemorrhage, should refrain from all respiratory exercises. Following a hæmoptysis all respiratory exercises with movements of arms should be prohibited, at least for a time. On the other hand I encourage quiet and deep respiratory movements, a few at the time, following a hæmoptysis. In cases where the sanguine expectoration has continued for weeks these deep, quiet respirations seem to have acted as a veritable styptic. Irritating cough resulting from the attempt to carry out the breathing exercises, or pleuritic pains resulting from the tearing of old adhesions, are no contraindications to the continuation of the respiratory exercises. Both cough and pain will cease in a short time. As long as the patient has learned to breathe properly through the nose and the air is relatively pure, cold, warmth, rain, snow and even wind should not prevent the patient from carrying out the physician's instructions for breathing exercises.

At times there are cases in which you desire to direct your respiratory exercises, so as to develop more particularly either the right or left lung. Under such conditions I have been in the habit of temporarily strapping the healthy side of the chest with the aid of adhesive plaster. Since coming to Baltimore my attention has been called to a much simpler and equally efficacious method, namely that of Naunym. I take the liberty to demonstrate this exercise before you, and take particular pleasure in doing so, for I am indebted for this acquisition of knowledge to your distinguished teacher, Professor Osler. He showed me that by sitting in an ordinary chair, with the healthy side of the chest pressing against the back of this chair, one could almost immobilize temporarily the healthy side, and by a deep respiration inflate the opposite lung to a much greater extent than would be possible without this fixation. Prof. Osler told me of what good service this method had been in patients convalescent from an empyema. I have been experimenting since in my room at the hotel and have learned that all chairs are not suitable for this excellent exercise. A chair with a concave back is utterly useless for that purpose. Naunym's breathing exercises for developing the right or left lung separately can best be carried out with an ordinary chair, with a seat low enough for the patient to fix his feet solidly on the floor. The back should be straight or moderately convex, and low enough to enable the patient to fix the top of it in his axilla, putting

his arm over the back and taking a firm hold of the seat from the outside. All the other directions for proper breathing, such as closed mouth, head erect, unrestricting clothing, are of course as important for this exercise as for any other. A second expiratory effort which we will describe presently may also be added to enhance the good effects of Naunym's exercises.

In all chronic forms of tuberculosis I have found the above described ordinary respiratory exercises of the greatest value. To increase their efficiency I have added a few movements to my armamentarium. While we need not be over-careful and over-precise when teaching respiratory exercises to a relatively healthy child, or young man or woman, in order to develop the chest capacity and respiratory function in the tuberculous patient we cannot be too careful in this matter. Not only the consumptive's physical but also his psychic condition demands that our prescriptions for respiratory exercises should be considered as important as the administration of any medicinal substance. In the modern teachings of phthisiotherapy air, air, and air again holds the first place, and to utilize as much as possible of this valuable substance we must not only have our consumptive patients live outdoors all day, resting either on a reclining chair or exercising by judiciously gradated walks, and at night have him sleep with the window wide open, but we must also see that he gets as much as possible of the good, fresh air into his lungs. I therefore add to the ordinary exercises an additional movement by having each respiratory act, that is to say, after a deep inspiration and corresponding expiration, followed by a second forced expiratory effort. This is for the purpose of expelling as much of the supplemental air as possible, which may be effectually aided by supinating the arms and pressing the thorax with them.

Considering that the amount of tidal air—that is to say, the volume which is inspired and expired in quiet respiration—is only 500 cc., the complemental air—the volume which can be inspired after an ordinary respiration—1500 cc., and the supplemental or reserve air—the amount which can be forcibly expelled after an ordinary respiration—amounts to 1240 to 1800 cc., one can readily see the value not only of deep breathing, but particularly of this second expiratory effort.

I may, perhaps, be permitted here incidentally to make a few remarks on the deficient respiratory function of the apices. The fact that in the majority of cases the tuberculous process begins at the apices has been explained by the supposed bad inspiratory function of this part of the lungs. Now, I agree in this respect with Hanau,¹ and consider the almost universally adopted statement of the deficient inspiratory function of the apices erroneous. On the contrary, these portions of the lungs inspire excellently well, almost too well, for dust and all sorts of micro-organisms enter there most easily and are found in large quantities in careful post-

¹ Hanau, A., Zürich, "Beiträge zur Pathologie der Lungenkrankheiten." (Zeitschr. f. klin. Medicin, xii, 1887).

mortem examinations. What is faulty is the expiratory function of the apices. A thorough expiration followed by a forced expiratory effort, as just described, is, to my mind, the only possible way to improve this defect and prevent stagnation and congestion, which, as is well known, form excellent media for the development of bacilli.

I will lastly demonstrate before you systematically the four or six exercises which I prescribe to my tuberculous patients according to their condition. To exercise No. 1, which for pedagogic purposes consists simply in raising the arms to the horizontal during the act of inspiration and to lower the arms during the act of expiration, I add the following: I instruct the patient, while his arms are stretched out in the horizontal position, to count three silently and slowly by moving the hands up and down, and then lower the arms during the act of expiration. Following this without inhaling again, he makes a second expiratory effort, as described. This second expiratory effort is not easy to teach and some patients are not able to learn it at all. Why, I cannot tell, but I usually succeed, at least in a measure, by having the patient say the word "ineh," prolonging the vowel during the attempted second expiratory effort. To the second ordinary exercise, where the patient raises his arms above his head, I add a bending backwards of head and thorax while the patient retains the air. This bending backward and coming back to the original position requires about five seconds; and the exercise is again followed by the second

expiratory effort. This exercise will also tend to overcome the habit of stooping. The third or swimming exercise, which you can only use for the tuberculous patient nearing recovery, may also be made more efficacious by a good vigorous second expiratory effort. The fourth respiratory exercise with rolling the shoulders which, as has been said, can be taken without attracting attention on the reclining chair, while walking or riding, should also be followed, whenever possible, by a second expiratory effort. This is an equally good exercise for patients in bed.

In teaching these breathing exercises I have not attempted to classify abdominal and thoracic breathing. For individuals predisposed to tuberculosis, consumptives and other bad breathers, abdominal and thoracic breathing should be combined to assure the greatest possible play and expansion of the lungs.

The value of respiratory exercises is now conceded by all phthisio-therapists. To assure a good, complete hæmatisation, that is to say, as nearly as possible a perfect oxygenation of the blood, to relieve the congested lungs of mucus and facilitate expectoration, diminish inflammatory exudates, in short, improve the respiratory and circulatory processes in the tuberculous patients, or those suffering from similar diseases, I know of no better means than judicious and regular breathing exercises under the supervision of a well trained physician.

16 West Ninety-fifth Street.

PULMONARY TUBERCULOSIS IN BALTIMORE.¹

BY H. WARREN BUCKLER, M.D.

A study of the mortality records of any of our large cities shows Pulmonary Tuberculosis or Consumption to be the most prevalent as well as the most fatal disease existing to-day. It causes about one death to every ten, and its victims average between the ages of 15 and 60, the best periods of one's life. With the exception of pneumonia and cholera infantum phthisis causes more deaths per annum than any other three diseases with which man is afflicted. During the past twenty-five years, from 1875 to 1900, there have been in Baltimore more than 28,479 deaths from phthisis, to say nothing of the deaths due to other forms of tuberculosis. The total mortality for the same period has been 222,562, making a ratio of 12.8%. During the past five years the death rate has been a trifle lower, owing no doubt to the greater ease with which we are able to recognize the disease, and to arrest its progress in its incipient stage. By years the rate is as follows:

Year.	Phthisis.	Total Mortality.	Percentage.
1895	1.141	10,301	11. %
1896	1.222	9,919	11.3
1897	1.047	9,329	11.2
1898	1.061	10,385	10.2
1899974	10,152	9.6

¹ Read before The Lænnec, a Society for the Study of Tuberculosis, January 30, 1901.

Of the 10,700 persons who died last year in this city, 1050 were victims of pulmonary tuberculosis, whereas scarlet fever, diphtheria and typhoid fever, three diseases usually dreaded, were together accountable for only 490 deaths. A comparison of the death rate of Baltimore with those of a few of our principal cities is not at all unfavorable, especially when one considers our large negro population, among whom the disease is especially fatal. The following chart, made from the tables of vital statistics of the several cities, shows the number of deaths, resulting from phthisis during the past year with its relative percentage to the total mortality.

Name of City.	Total Mortality.	Phthisis.	Percentage.
Baltimore	10,700	1056	9.8%
New York	70,872	8,155	11.5
Philadelphia	25,078	2,717	10.8
Chicago	21,809	2,514	11.3
Boston	11,154	1,289	11.5
Dist. of Columbia.	6,026	.758	12.5

The above will show that Baltimore, even with its 80,000 or more negroes, is not the hotbed of tuberculosis as many would believe, and when we consider that for the past few years every effort has been made in many of these cities to reduce the mortality from phthisis, whereas in Baltimore practically nothing has been done, the comparison is still

more comforting. In order to have a more definite idea of the disease as it exists to-day in the city, I have endeavored to study the conditions in the different wards and districts with the hopes of getting an idea of the relative prevalence of the disease in the several sections of the city. This I have found to be extremely difficult as there are at present no means of ascertaining either the number or the location of cases. It has been estimated that there are to-day about 10,000 consumptives in the city, and until some method of notification of registration is adopted, it will be impossible to study the distribution of the disease except through acquaintance of small areas personally visited or from a study of the annual death list.

Through the courtesy of Dr. C. Hampson Jones, our assistant health commissioner, I have been privileged to show you this evening a map prepared by him, showing the exact location of every death from pulmonary tuberculosis from January 1, 1900 to January 1, 1901, copied directly from death certificates on file in the office of the health department. On this map the white pins represent the deaths among the whites, and the black pins give us an idea of the ravages of the disease among the negroes. The city, as you see, is divided into twenty-four wards, varying in population from 16,500 to 35,000, and containing from 2500 to 9000 dwellings. The ninth, eleventh, twelfth, sixteenth, seventeenth, eighteenth and nineteenth are largely suburban, although comparatively thickly settled in some portions. In these wards where fresh air and sunshine are plentiful, the death rate from tuberculosis is low, averaging during the past year only about six per cent. The only region to which I wish to call your attention in these outskirts of the city is Hampden, a small village settlement between Jones' Falls and Woodberry, and populated largely by mill hands. In this neighborhood there occurred last year seventeen deaths from pulmonary tuberculosis, and I personally at present know of four cases from this suburb undergoing treatment at the Johns Hopkins Dispensary. Notice how few cases occur in the neighborhood of Clifton, Druid Hill Park, Walbrook and Irvington, all localities fully as thickly populated. It is interesting to know how few deaths have occurred in the extreme southern sections of the city and around Locust Point. These are all regions thickly settled, occupied by laboring people, in some houses very much crowded, and living under the most unhygienic surroundings. Yet you see that only three deaths resulted from phthisis during the past year in this part of the city. This I believe, is due to the existence of the large gas works which impregnate the air with fumes from their furnaces, thus rendering it, to a certain extent germicidal. I have been informed by practitioners of this neighborhood that consumption is of extremely rare occurrence in this part of the city, and this explanation seems interesting as well as satisfactory.

The part of the first ward bounding the basin and containing the shipping and dirtiest business section of the city, and the second ward, in which are located the great majority of shops, warehouses and public buildings, have a compara-

tively low death rate from phthisis, owing to the small population and few dwellings.

One could not have better proof that tuberculosis is essentially a filth disease, flourishing in unhygienic surroundings, than to know how practically exempt from the disease the better residential sections of the city are. For example in the 13th ward, in an area bounded by Franklin Street on the south, North Avenue on the north, Park Avenue on the east and Jones' Falls on the west, there have been no deaths during the past year from tuberculosis. Again in the 15th ward, in the neighborhood surrounding Eutaw Place, between Druid Hill and Park Avenues, there have been no cases of phthisis reported to the health authorities. But to the west of Druid Hill Avenue, where our melanotic citizens predominate, the death rate from consumption is little short of appalling. In the 14th ward, with an estimated population of 23,000, there are 12,000 or more negroes. The death rate from tuberculosis in this ward for the past year was a trifle over 18%. There is scarcely a block in this ward in which there has not been reported a consumptive death during the past year. Quite recently I have been making a house to house visitation in some of the neighborhoods especially infected, and the results promise to be most interesting. In one house especially I have found that during the past two years there have been three deaths from tuberculosis in one family, which had previous to the occupation of this house been perfectly healthy. Upon questioning the neighbors, I learned that the previous occupant had died of lung trouble shortly before the present family moved in. A small triangular section, bounded by Richmond, Cathedral and Biddle Streets, is an area of considerable interest, as it is a part of the city familiar to most of us, and also because it serves as an especial menace to those portions of the city previously mentioned as being free from the disease. In this small area there were ten deaths during the past year from phthisis, seven blacks and three whites. I would like to call your attention to the 10th ward, one of the smallest of the city, bounded by Jones' Falls, Preston, Caroline and Monument Streets. This little ward has a greater population per acre than any other ward, with a total death rate of about 500, and a percentage from phthisis, of about 15%. The adjacent ward, the 8th, in which this hospital is located, one of the largest wards of the city, has the greatest number of actual deaths per annum from tuberculosis, averaging between 90 and 100. But a correspondingly large total mortality brings the ratio down 10%. This ward has about the same population as the 10th, but scattered over an area of nearly twice the size, and occupying four times as many dwellings. Does it not therefore seem probable from the above that overcrowding, poor ventilation and lack of fresh air and sunshine are not the sole causative factors in the spread of the disease, but that certain districts seem to be more especially tainted with tuberculous infection than others, and that to a certain extent, where one lives seems to be as important as how one lives. The degree of elevation has seemed to have little effect upon the distribution of the disease. The difference

between sea level and the highest point in the city is only that of a few hundred feet, and as I have already shown some of the worst infected districts are in sections of the city comparatively high, whereas in the neighborhood of the water front and Locust Point the disease is of unusually rare occurrence.

What may be the best practical methods of reducing the dangers from tuberculosis are problems of such enormity as to be entirely beyond the scope of a paper of this length, suffice it to say that it is only a question of time before our municipal authorities will be forced to adopt stringent regulations, such as have proven successful elsewhere in checking the spread of the disease. Maryland, unlike many of our States, has as yet done nothing, but the legislatures of New York and Pennsylvania have already passed laws requiring registration of all cases of tuberculosis at the offices of the

health department, thus placing consumption upon the list of notifiable diseases. Dr. Herman Biggs, of the New York health department, at present estimates that he is enabled to have under surveillance 9/10 of all phthisical subjects. By forcing some and by teaching others to properly dispose of their expectorations, and by disinfecting the quarters of the patient after death, he believes that he has in the past six years reduced the mortality nearly 35%, which means the saving of 1500 lives annually. If to this society can be given the credit of stirring up in Baltimore such interest as may be necessary to insure the adoption of similar preventive measures, surely the idea which originated its foundation will have been a happy one.

N. B.—The numbers and boundaries of the city wards referred to in this paper are those which were in existence at the time of its first presentation.

CONCERNING A DEFINITE REGULATORY MECHANISM OF THE VASO-MOTOR CENTRE WHICH CONTROLS BLOOD PRESSURE DURING CEREBRAL COMPRESSION.¹

BY HARVEY CUSHING, M. D.

During the course of a long series of observations undertaken for Professor Kocher in the Physiological Institute of Bern in an attempt to elucidate certain questions of dispute regarding the circulatory phenomena which are consequent upon cerebral compression, it has been observed that there is a constant tendency on the part of the blood pressure to remain at a level above that of the pressure exerted upon the brain.

The fact that cerebral compression occasions a rise in blood pressure is universally known but it does not seem to have been recognized that the degree of this elevation occurs *pari passu* with the degree of compression (measured in millimetres of mercury) to which the medullary centres are subjected. It is ordinarily stated by the numerous experimenters who have dealt with problems of compression that fatal symptoms originate when the intracranial pressure approaches or reaches the height of the arterial tension. The fact that the arterial tension is a varying quantity which regulates itself so as to overcome the effects of the increased intracranial pressure seems never to have received attention.

In the greater number of my early observations the experimental compression has been made by means of quicksilver which was allowed to enter a thin rubber bag at the end of a metallic canula which was screwed into a trephine opening in the skull. By this method it was impossible to estimate with exactitude the degree of compression exerted against the medulla since the elasticity of the bag, the resistance of the dura in spite of its preliminary liberation from the skull, and the fact that the brain does not transmit the pressure from such a localized foreign body equally in all

directions were always elements of uncertainty in the calculation. Nevertheless the method sufficed to call attention to the fact above mentioned, namely, that when the degree of compression was increased so as to exceed that of the blood pressure the latter would in turn almost invariably rise to a level exceeding that of the intracranial tension. In this way the blood pressure could be carried to indefinite heights, occasionally to 250 mm. of mercury or more, and be held there until the centres in the medulla became permanently fatigued.

The suggestion thus offered as to a definite regulatory mechanism which counteracts the compression anæmia by elevation of blood pressure was further strengthened by direct observation, of the cerebral circulation through an accurately fitting glass window inserted in another trephine opening under which the dura had been opened. When the intracranial tension had been carried up to the point of blanching the convolutions and indeed of obliteration of the pial arteries themselves, it could be seen through this fenestra that this condition of anæmia was but a transient one, since in a few seconds the vessels would once more fill and the circulation become reestablished. On some occasions, to be explained later, the circulation could be seen to appear and disappear with rhythmic periodicity, the intracranial tension meanwhile remaining at the same level.

The opportunity of testing the truth of the hypothesis thus suggested has been offered in the *Laboratorio di Fisiologia* of Turin² where a simple but more graphic method of

¹ Reprinted from the Archives Italiennes de Biologie for 1901.

² I am deeply indebted to Professor Mosso in Turin and to Professor Kronecker in Bern for extending to me the privileges of their laboratories while carrying out these observations.

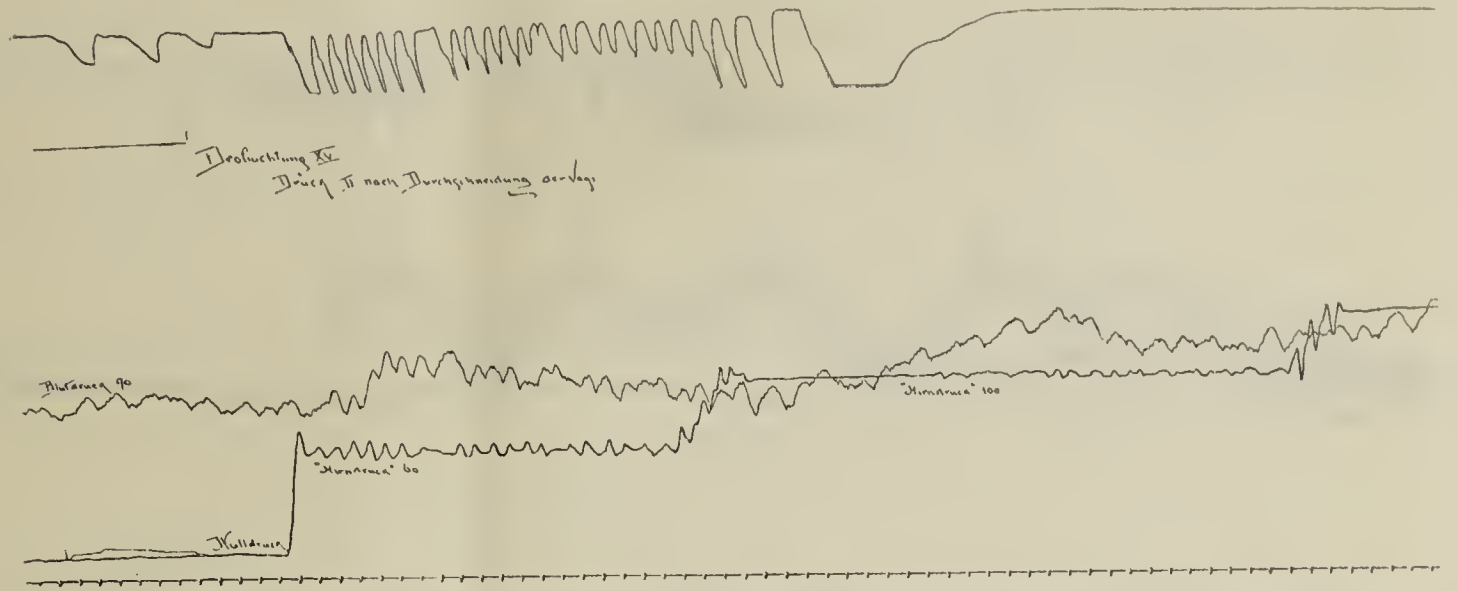


CHART II.—After division of the vagi. Intracranial tension ca

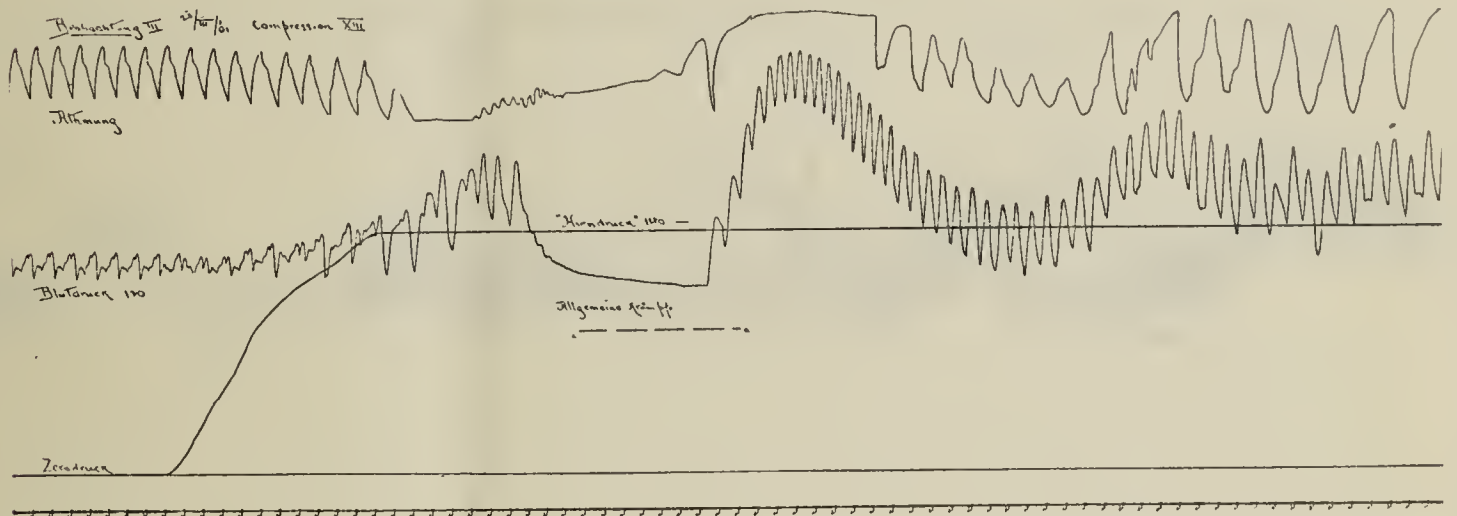


CHART III.—Animal in normal condition. Intracranial tension brought rapidly to the point of exc the usual temporary vagus inhibitory effect.

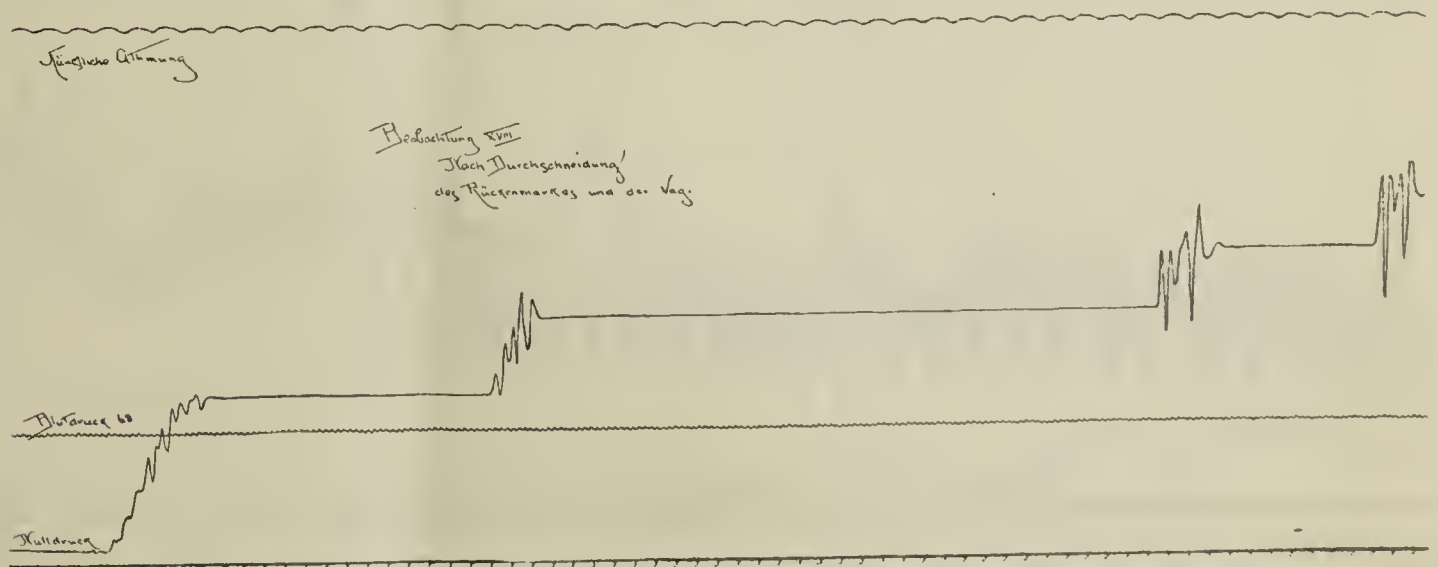
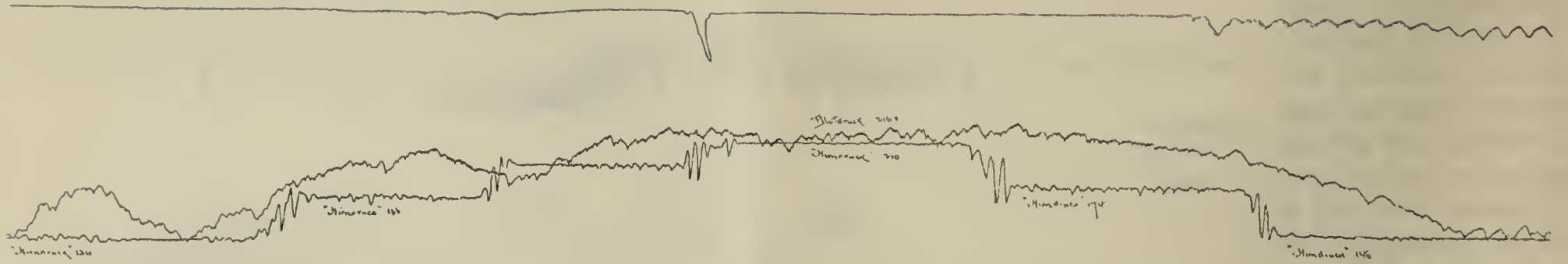


CHART V.—After section of both vagi and spinal cord. Increase of intracranial tension to 192 mm. with



ried to 210 mm. of Hg with a corresponding rise in blood pressure from its normal level at 90 to 216.

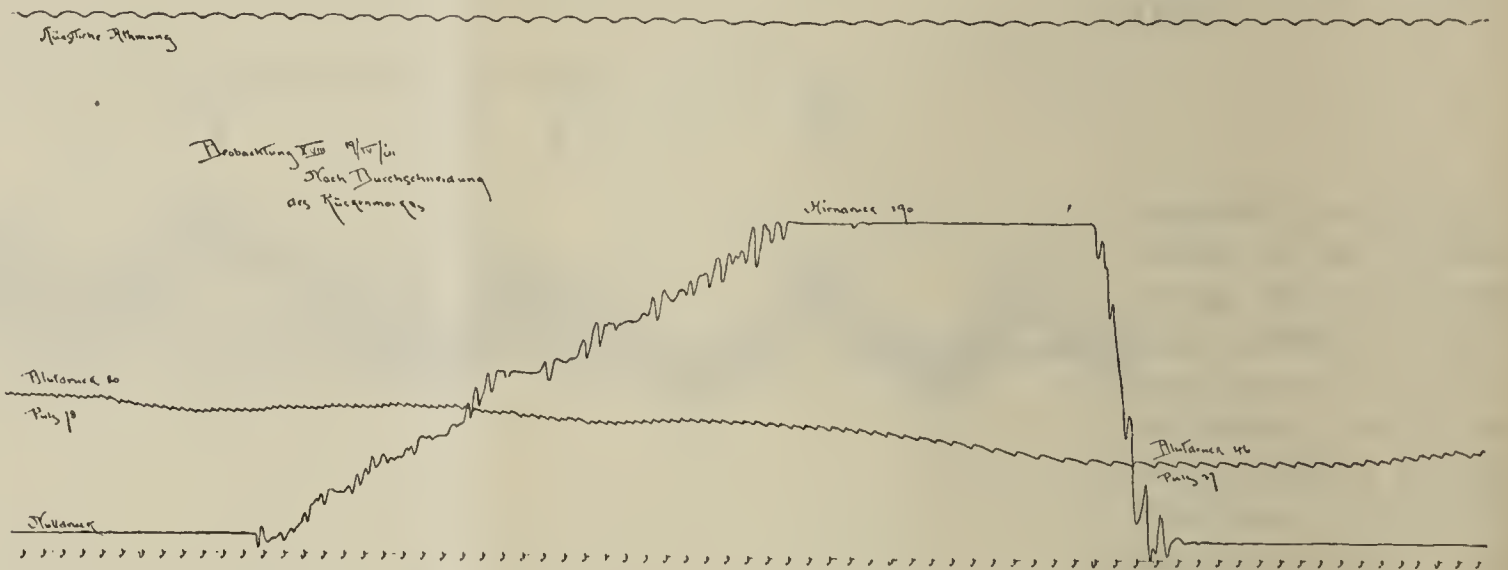
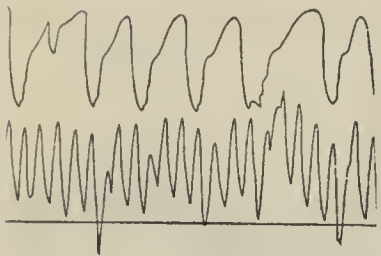
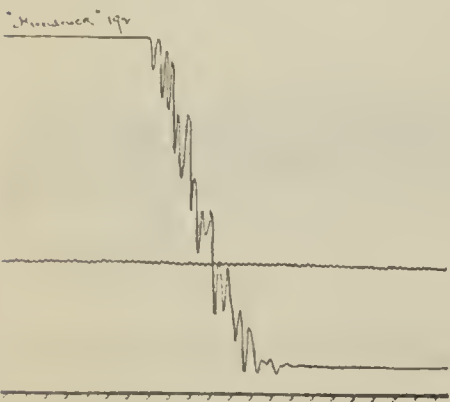
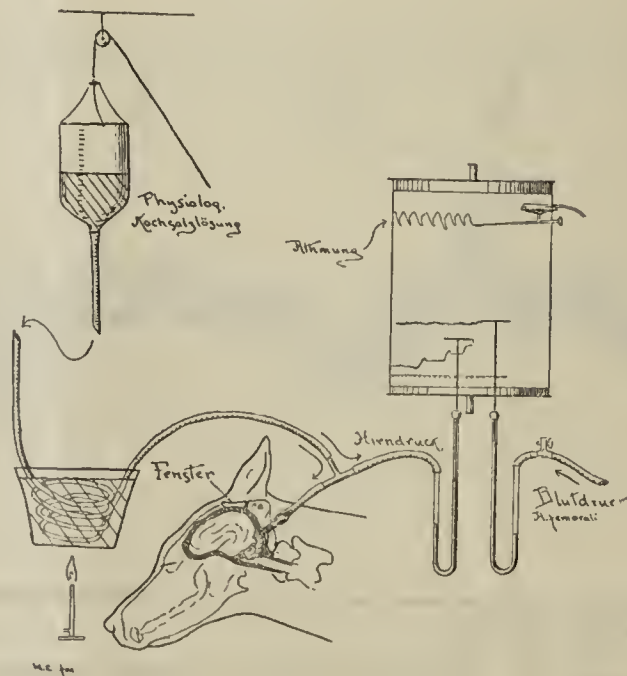


CHART IV.—After section of the spinal cord. Increase in intracranial tension without production of rise in blood pressure. Vagus effect alone.

eeding blood pressure with



out influence upon blood pressure.



Sketch showing arrangement of apparatus as used in these experiments

demonstrating this coincidence of blood pressure and degree of intracranial tension has been employed. In this Turin series of observations the animals employed have been invariably dogs. In Bern the same phenomena have been observed in other animals.

Method of Experimentation.—A preliminary injection of morphia has been given and the animals have been lightly anesthetized with ether.

Blood pressure has been recorded from the femoral artery lest the ligation of one of the carotids should in any way disturb the intracranial circulation.

For direct observation of the circulatory condition of the brain a large trephine opening has been made in the median line in such a situation as to avoid the large emissary veins which pass between dura and diploë not only from the great lateral cerebral veins anteriorly but posteriorly from the torcular itself. The dura is opened to one side of the longitudinal sinus exposing part of a convolution, its limiting sulci and the pial vessels. In the trephine opening an accurately fitting glass window is inserted through which the degree of distension or compression of the longitudinal sinus (unless the animal be very old), the condition of the capillary circulation in the exposed convolution and the vascularity of the pial vessels can be beautifully seen during the subsequent experiment.

The intracranial pressure has been produced and recorded as follows. Another, much smaller trephine opening is made over one part or another of the cerebrum, cerebellum or cord (in the latter case by trephining the lamina of one of the vertebrae). The underlying dura is carefully and freely opened. In the trephine hole an accurately fitting metal canula is screwed to which a firm rubber tube is attached communicating with a flask of physiological salt solution so arranged that it may be raised or lowered for the production of pressure to any desired level (cf. sketch). The rubber tube leads through a basin of hot water so that the fluid entering the cerebro-spinal space may be approximately at body temperature. The tube furthermore communicates with a mercury manometer which thus registers the degree of intracranial tension. In this way the cranial cavity is converted into a plethysmograph and the volume-pulse as well as the tension of the liquor can be graphically represented.

The blood pressure and intracranial tension may thus be recorded side by side on a kymographion, the manometers being so arranged that the zero pressures are taken from the same abscissa, (of sketch).

Respiration and time, the latter with a two second interval, are also recorded on the charts.

By the devices ordinarily made use of for the production of cerebral compression, especially by the introduction over the hemispheres of circumscribed bodies, solid or otherwise, no exact indication of the degree of pressure over the medulla is given since it is well known that pressure so applied is not transmitted equally throughout the three large cerebral

chambers which are limited by tentorium and falx. In some animals indeed the brain may be so dislocated that the medulla may to a large extent be crowded through the foramen magnum and the vaso-motor centre thus partially escape from the compression effects to which the cerebrum is subjected. For this reason it was essential for our purposes to employ a method in which the intracranial tension over the fourth ventricle was to all intents and purposes equal to that which we were measuring in millimetres of mercury at the point of application of pressure. In no other way could an accurate comparison with the blood pressure be made.

It might be supposed and has heretofore been stated that the extraordinarily free communication between the cerebro-spinal space and the cranial venous circulation would lead to a rapid overfilling of the right heart, should a continuous supply of artificial liquor under an abnormal pressure be afforded. As a matter of fact during life and when the blood pressure remains above that of the intracranial tension this escape of liquor is not exceedingly rapid. During a long experiment with the intracranial tension of this fluid varying from one to two hundred millimetres of mercury and so held from ten to twenty minutes at a time, on an average only 80 to 100 cc. of the salt solution would be taken up by the circulation, certainly not enough to alter the reliability of the observations. On the other hand, after the death of the animal with a zero blood pressure the liquor enters the veins and thus the heart with much greater rapidity.

Care must be taken that the dura corresponding to the trephine opening for the canula be accurately excised and that the compression fluid be not allowed to enter from a high pressure with too great abruptness since under such conditions the dura may be flattened against the brain and the fluid collect as a foreign body between the membranes and skull instead of passing freely in all directions over the entire central nervous system. Under these latter circumstances and provided that the pressure from without is kept at a constant level the tension of the fluid in the cerebro-spinal space is the same throughout and the absorption which is in too small amounts to embarrass the cardiac action, may be disregarded. Thus, very slight, if any, differences can be observed in the regulatory mechanism to be described, whether the fluid be allowed to enter primarily, over cerebrum, cerebellum or cord.

The accompanying charts demonstrate more plainly than can any description the striking regulatory phenomena on the part of the blood pressure, as controlled by the vaso-motor centre, which occurs during varying degrees of medullary compression.

Until the intracranial tension ("*Hirndruck*") exceeds that of the blood pressure, nothing more than the usual slight excitatory phenomena (cf. Chart I) are seen, indeed if the fluid enters easily without compromising the sensitive dura this primary quickening of pulse and respiration may be absent (cf. Chart III.)

When, however, the pressure is increased until it exceeds that of the blood pressure and especially if this high intracranial tension has been rapidly produced (as in Chart III) we may occasion momentarily the so-called major symptoms of compression with Kussmaul-Tenner spasms, evacuation of bladder and rectum, practical cessation of respiration and pronounced vagus effect upon the heart often with a complete "Stillstand" lasting from ten to twenty seconds. Then follows a release from this extreme vagus inhibition and the vasomotor centre begins to exert its striking influence.

In the more simple condition when the pressure has been increased more slowly (Chart I), these vagus symptoms are often avoided and the rise in blood pressure follows immediately upon the increase of "*Hirndruck*" to a level which temporarily exceeds it. Under these circumstances and when there has been no pronounced vagus effect (as in Chart III, where the sudden release from vagus inhibition has temporarily let the vaso-motor action run away with the blood pressure) it can be seen that the rise in blood pressure is merely sufficient to carry it above the level of the compression fluid, in other words an arterial pressure is called out which suffices once more to carry blood to the centres in the medulla. If, as in Chart III, an unnecessary elevation of blood pressure has primarily been occasioned it will fall and continue along a line representing a level slightly above that of the compression. Should the intracranial tension be again increased the same phenomena will be again repeated (cf. Chart I), and in this way the blood pressure may be forced to a level considerably over 200 mm. of mercury before the vaso-motor centre shows signs of giving way and fails to respond to the demands of an anæmic medulla. Within reasonable limits of compression, however, this compensatory action may be indefinitely prolonged.

On many occasions, as in Chart I, the blood pressure may be seen to rise and fall, above and below the line representing the degree compression, with a rhythmic periodicity of one form or another (Traube-Hering waves, etc.). This phenomenon is readily explained by observation through the glass window of the circulatory condition of the brain, a state of absolute anæmia accompanying those periods when the blood pressure is below the level of the compression line, an abundant circulation being present when it is above. As the average line of blood pressure is raised to a higher level by increasing again the degree of intracranial tension it carries with it this same rhythmic activity (cf. Chart I).

It is the object of this communication merely to state the existence of the regulatory function above described, and the

writer makes no pretense at theorizing over the physiological laws which govern it. However, the following observations demonstrate that the process depends largely for its action upon the vaso-motor centre and the control which the latter exerts over the great splanchnic circulation.

1. If the vagi be divided and compression subsequently be made upon the brain, the blood pressure will be seen to correspond even more closely than before to the degree of intracranial tension (cf. Chart II) always remaining slightly higher than the pressure exerted against the medulla or else passing above and below it with wave-like rhythm. The vagus effect (as shown in Chart III) of course is absent under these circumstances.

2. If a coil of small intestine be exposed, during such a compression experiment as has been described, the splanchnic vessels can be seen to contract during the rise in blood pressure and to dilate once more as the latter falls at the end of the experiment.

3. Again if through a trephine opening in the atlas the spinal cord be divided with a blunt instrument so as to occasion the slightest possible bleeding, and then pressure be applied, the vagus effect alone will be forthcoming with no rise in blood pressure (cf. Chart IV), at least until the independent spinal centres shall have asserted their individual activity, when a slight rise may be occasioned.

4. If both vagi and cord be thus divided an increase in intracranial tension does not affect in the slightest degree the level of blood pressure (cf. Chart V.)

5. Similarly cocaineization of the medulla by the introduction of the needle through the occipito-atlantal ligament, throws out the action of the bulbar centres. Under these circumstances, if artificial respiration be instituted the animal may live with a temporarily paralysed vaso-motor centre and an increase of intracranial tension does not affect the blood pressure until the cocaine effect begins to wear away.

As a result of these experiments a simple and definite law may be established, namely, that *an increase of intracranial tension occasions a rise of blood pressure which tends to find a level slightly above that of the pressure exerted against the medulla.* It is thus seen that there exists a regulatory mechanism on the part of the vaso-motor centre which, with great accuracy, enables the blood pressure to remain at a point just sufficient to prevent the persistence of an anæmic condition of the bulb, demonstrating that the rise is a conservative act and not one such as is consequent upon a mere reflex sensory irritation.

THE JOHNS HOPKINS HOSPITAL BULLETIN.

The Hospital Bulletin contains details of hospital and dispensary practice, abstracts of papers read, and other proceedings of the Medical Society of the Hospital, reports of lectures, and other matters of general interest in connection with the work of the Hospital. It is issued monthly.

Volume XII is in progress. The subscription price is \$1.00 per year. The set of twelve volumes will be sold for \$23.00.

PENDULOUS TUBERCLES IN THE PERITONEUM.

BY W. G. MACCALLUM, M. D.

As has long been known, there are formed in the Perlsucht or peritoneal and pleural tuberculosis of cattle masses of various sizes, of caseous or calcified material surrounded by a fibrous capsule and embedded in a loose proliferated connective tissue arising from the subperitoneal tissue. These masses often reach very considerable dimensions, and from their weight become pendulous, drawing out the underlying tissue into a stalk—often there are adhesions and such band-like adhesions bearing several caseous nodules have somewhat the appearance of a string of pearls, whence the name. Virchow's¹ illustration and description of this condition are very accurate, although he considered it a form of lymphosarcoma.

In human beings, however, such a form of tuberculous peritonitis is not so common, and I have been able to find in the literature the description of only one such case; Bizzozero,² who describes this case was unable to find records of a similar case, and in the admirable reviews of the recent literature by v. Brunn,³ there is no mention of such a condition.

Bizzozero's case was that of a young peasant 24 years old, who died with the diagnosis of pulmonary tuberculosis. At the autopsy the lungs were found to contain masses of conglomerated tubercles, and there were already cavities at the apices. In the peritoneal cavity was a litre of seropurulent fluid and the intestinal loops were firmly adherent to one another and to the liver by means of a yellowish exudate, which was also found between the liver and the diaphragm. On removal of this exudate covering the intestines, it was found that the peritoneum, both visceral and mesenteric, was covered with most numerous whitish tuberculous nodules of the size of the finest grain of millet to that of a pea. Sometimes they united to form a plate of the size of a five lira piece. Numerous tubercles were found in the parietal peritoneum and subserous connective tissue also. The mesenteric glands were enlarged—microscopical examination shows in them the usual tuberculous detritus.

The mucosa of the stomach was normal, but in the ileum it was pigmented, and numerous tuberculous ulcers corresponding with which there were especially numerous tubercles on the peritoneum.

More careful examination of the peritoneal tubercles—especially those of the mesentery, demonstrated that their

nature was varied enough. Some were embedded in the tumefied peritoneum and showed only as spots of rather white color—others produced a sensible elevation—others projected by their whole height above the level of the peritoneum—finally others were not attached at their point of origin except by a peduncle of a length varying from a millimetre to a centimetre, and varying in diameter from 1 to $\frac{1}{3}$ or $\frac{1}{4}$ of a millimetre—often the peduncle was flattened together, so that with a width of $\frac{1}{2}$ centimetre it might have a thickness of only $\frac{1}{3}$ to $\frac{1}{10}$ millimetre. The histological constitution of the tubercles immersed in the peritoneum and those with peduncles was the same, and as usual had outside a layer of connective tissue in active proliferation and internally the elements in detritus and fatty degeneration.

"The microscopical examination of the peritoneum," he says, "shows me the probable reason why, while in other cases of tuberculosis the small neoplasms are adherent to the peritoneum, in mine they were for the most part pedunculated. The preparations show that the connective tissues of the membranes were separated by an abundant hyaline fundamental substance in which were numerous new-formed cells, of which some were spherical or oval, others fusiform or stellate—naturally the peritoneum, tumefied and softened by the presence of superfluous fundamental substance and of numerous new-formed cells could not support the weight of the tubercles, and yielding, formed of necessity a peduncle.

"The layers of muscular fibres have taken no part in the new formation. Only in the interfascicular connective tissue was there proliferation of cells.

"This case leads me to believe that, in all probability, tubercles might also produce a kind of free body in the peritoneum, as is the case with fibromata, lipomata, etc., and even sclerosed appendices epiploicae (Virchow, *Krankh. Geschw.*, i, p. 384).

The case which occurred in this hospital was that of a white woman, aged 38, who died with symptoms of pulmonary tuberculosis.

At the autopsy, the peritoneal cavity was found to contain no excess of fluid, and the peritoneal surfaces were smooth and glistening. There were, however, nodules lying just under the serous surface, scattered over both parietal and visceral layers. These had a most extraordinary arrangement—they varied in size from 1 or 2 mm. to 2 cm. in diameter. Some were sessile and flattened and projected only a few mm. from the general peritoneal level, but most of the nodules hung free, each in a sort of long blind tube

¹ Virchow, *Krankh. Geschwülste*, ii.

² Bizzozero, *Morgagni*, vol. ix, 1867.

³ von Brunn, *Centralbl. f. Allg. Path. u. Path. Anat.*, Bd. xii, No. 1 and 2, 1901.

formed apparently by the drawing out of the peritoneum into a tubular pedicle. Some of these pedicles reached a length of 10 to 12 cm., although most of them were much shorter and broader. The long ones generally took their origin from a wide uplifting of the peritoneum, and in some part of their length they were often narrowed to a width of only 1 to 2 mm., when they became much twisted and tangled with one another. All of these pedicles contained fluid which if the terminal caseous nodule were allowed to hang down, ran downward to the end of the tube, distending it to a globular ball; by elevating the end, the somewhat reddish fluid could be made to run back and spread out under the peritoneum over the intestine and perhaps even to enter another tubular pedicle. In one or two cases such tubular prolongations show no caseous mass at the end, and indeed one elongated sac with extremely thin, delicate walls and clear, yellow fluid contents was found entirely free in the peritoneal cavity. This body tapered to a point at each end and, as described above, the fluid could be allowed to run to either end, forming a globular bubble-like distended mass, the remainder collapsing into a delicate string. In some cases large sessile caseous masses were found to be overlaid by a loose peritoneal film which formed part of the wall of the large pedicle of some other mass, and in others this uplifting of the peritoneum from the surface of the sessile nodules was incomplete, so that the peritoneal film appears to start from the middle line of the nodule—finally in some cases, small caseous nodules were found hanging by a stalk inside the elevated peritoneum.

The peritoneum thus drawn up was furnished with numerous widely dilated vessels—in some of the pedicles, however, undue twisting had produced strangulation, and the tissue had a dark purple color. Such pedicled nodules which were opaque and yellow, and on section showed large areas of caseation, arose from and were attached to any part of the peritoneum, parietal as well as visceral, and even from that covering the pelvic organs. The intestinal mucosa appeared normal except for two small ulcers in the cœcum opposite the attachment of one of the large subserous masses. The lymph glands in the abdomen were apparently not involved—lymph glands lying side by side with the caseous nodules showed, even when examined microscopically, no alteration. The cervical and mediastinal lymph glands, however, were almost entirely caseous.

The spleen and liver were bound to the adjacent tissues by old adhesions which contained caseous masses—tubercle-like nodules could be seen in their substance on section.

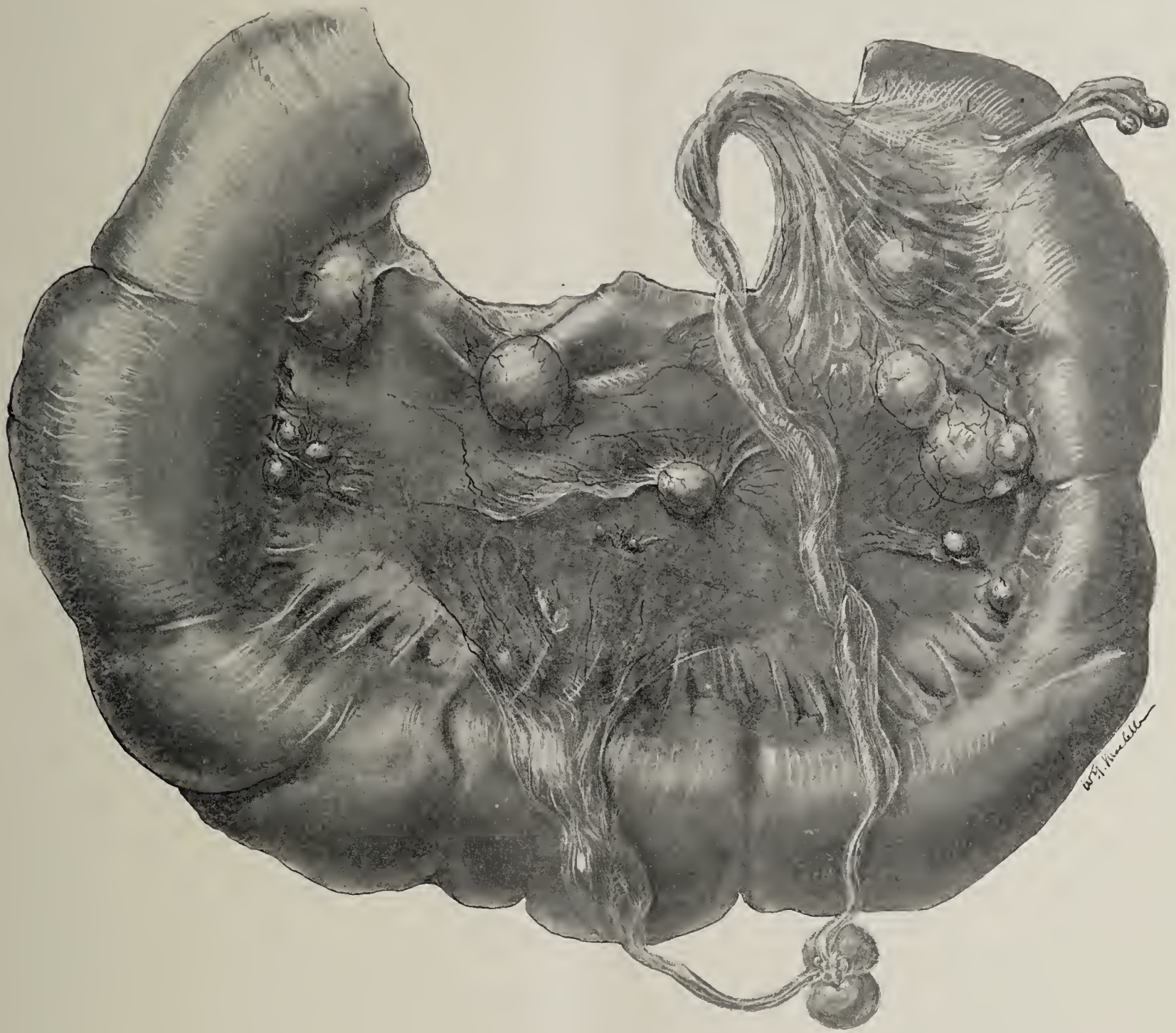
The lungs were bound to the costal pleura by old adhesions—they were somewhat emphysematous and studded throughout with minute miliary tubercles—the bronchial glands were not involved.

Finally there was a tuberculous leptomeningitis, the pia mater over the pons cerebellum and cerebrum showing here

and there a yellowish exudate with tubercles along the vessels.

Microscopically the nodules described in the liver, spleen, lungs, etc., proved to have all the histological features of tubercles.

Sections were made through the peritoneal nodules so as to pass through the pedicle and the underlying tissue. The nodules were necrotic with the exception of the peripheral portion which had the characters of a tuberculous tissue consisting of irregularly arranged epithelioid cells and giant cells with very numerous lymphoid cells—externally a considerable mass of elongated connective tissue cells formed the capsular layer over which lay the peritoneal endothelium—this last, however, not being always seen in the sections. The architecture of the more central portions was sometimes preserved enough to indicate that they had arisen from the confluence of several smaller tubercles. Tubercle bacilli were to be found in great numbers in these masses and especially in the zone between the living and necrotic tissue in which the cells were degenerating and their nuclei becoming fragmented. The sessile nodules are embedded in an extremely vascular tissue which indeed spreads out wide of them and really forms also the pedicles of the pendulous nodules. Microscopically this tissue consists of a very loose connective tissue, in the interstices of which lie numerous round and plasma cells, but especially characterized by the presence of enormous numbers of very wide, thin-walled blood-vessels distended with blood. This vascular tissue passes up over the nodules, being fairly sharply marked off from the tuberculous tissue of their substance, and its presence explains the appearance of the wide area of congestion about each nodule, and the vessels described above as ascending to pass over the surface of the nodule. Sections through a pedicle show the same richly vascularized loose tissue in the wide clefts of which runs the fluid described macroscopically as appearing to be contained in a tube. Such tissue has, as Dr. Welch suggests, great resemblance to the tissue found newly formed on the dura mater in chronic internal hæmorrhagic pachymeningitis and he further tells me that he has observed it in the peritoneum and especially in the pelvic peritoneum of women without any associated tuberculosis. Indeed, as stated above, there are in this case many vascular areas, and even elongated pedicles without tubercles, and many long pedicles support tubercles of only insignificant size which can scarcely be thought of as having, by their mere weight, drawn out the peritoneal tissue into its present form. So although at first the mechanical effect of the weight of the tubercles seemed to offer a probable explanation of these curious formations, it now seems much more plausible to accept the suggestion of Dr. Welch and to consider the tubercle masses as formed, in part at least, in preexistent loose adhesions and strands of vascular new-formed connective tissue, not denying the importance of gravity in altering the appearance of these strands when the mass had reached any considerable size, or in some cases of initiating their elongation.



The drawing shows a portion of the intestine, natural size, with its mesentery, from which arise the sessile and pedunculated nodules described.

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SUMMARIES OR TITLES OF PAPERS BY MEMBERS OF THE HOSPITAL AND MEDICAL SCHOOL STAFF APPEARING ELSEWHERE THAN IN THE BULLETIN.

FREDERICK H. VERHOEFF, M.D. A Case of Noma of the Auricles, Due to the Streptococcus Pyogenes, and its bearing on the Etiology of Noma in General.—*The Journal of the Boston Society of Medical Sciences*, Vol. V, pp. 465-478, May, 1901.

—— The Theory of the Vicarious Fovea Erroneous.—*The Ophthalmic Record*, June, 1901.

THOMAS B. FUTCHER, M.B. Syphilitic Fever, with a Report of Three Cases.—*New York Medical Journal*, June 22, 1901, p. 1065.

The importance of keeping in mind the fact that fever of obscure origin is occasionally due to syphilis is emphasized. With the onset of the secondary eruption there is nearly always an elevation of temperature. This "fever of invasion" is usually of a remittent type. Syphilitic fever, however, may

also be either continuous or intermittent in type. It may occur as early as four weeks previous to the appearance of the secondary eruption or as a late tertiary manifestation.

Syphilitic fever is frequently mistaken for malaria, typhoid fever, tuberculosis, sepsis and occasionally rheumatic fever. Attention is drawn to the importance of making a careful examination of the long bones and viscera for evidences of tertiary lues in all cases of fever, of obscure origin, also of administering potassium iodide and mercury as a therapeutic test.

The first case reported had an intermittent fever commencing four weeks before the onset of the secondary eruption. It resembled closely the fever of aestivo-autumnal malaria. The second case had a fever simulating typhoid and its true character was determined by the finding of periosteal thickenings and by the cessation of the fever after administering potassium iodide. The third case had an intermittent fever resembling malaria twenty-nine years after the contraction of lues.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

Monday, April 15, 1901.

The meeting was called to order by the president, Dr. Welch, who introduced Dr. Harvey R. Gaylord of the New York State Pathological Institute at Buffalo, who spoke on The Parasite of Cancer, with Demonstrations.

DISCUSSION.

DR. WELCH.—Dr. Gaylord has brought before us something more than the mere description of the so-called cell-enclosures observed in hardened specimens of cancer. Of the enclosures hitherto described in preserved material the only ones which present anything like a definite organization and which, it seems to me, have not been altogether satisfactorily explained are the bodies first accurately described by Thoma and Sjöbring, and subsequently noted by most of those who have studied this subject. These bodies in English and American writings are often designated without much propriety as "Plimmer's bodies." No conclusive evidence that these bodies, still less that any other of the various enclosures, are parasites, has been furnished, and it now seems evident that no further progress in the search for parasites is likely to be made by the examination of hardened material with our present methods.

Under these circumstances it is important to turn to the examination of fresh material and to make attempts to cultivate parasitic organisms, provided such exist in cancer and other malignant tumors. This direction of study has therefore been followed in recent years by several investigators, and it is especially his results along these lines which Dr.

Gaylord has reported to us this evening. As regards artificial cultures, it is certain that no forms of bacteria demonstrable by existing methods are directly concerned in the causation of cancer, and, notwithstanding the stronger claims made in behalf of Blastomycetes, I am glad to learn that Dr. Gaylord rejects these claims and takes a position in this regard opposed to that of San Felice, Roncali, Plimmer, Leopold, and others. He interprets as Protozoa the bodies which he regards as parasites.

Leaving out of consideration the occasional and accidental presence of cultivable bacteria and yeasts in cancer, I question whether what is called by Dr. Gaylord and other investigators as the cultivation of protozoa or of sporozoa from cancers should be so designated, and it does not appear that secondary cultures carried on from generation to generation have in any instance been secured.

There is not much agreement among the different observers either in the description or the interpretation of the various bodies regarded by them as parasites to be seen in fresh cancerous material or fluids, or in such material kept free from bacterial contamination, whether mixed with some cultural fluid or not. Dr. Gaylord lays especial emphasis upon the presence in cancers and other conditions of homogeneous, yellowish, spherical bodies resembling droplets of fat but without the usual reactions for fat, and he considers that he finds evidences of multiplication of these bodies and of their passing through a definite cycle of development which he describes. He is, I trust, prepared for a considerable degree of skepticism following this announcement of his results, and it is desirable that this should be the attitude of mind until we are in possession of more evidence than has yet been

furnished in favor of the parasitic hypothesis. It is, however, incumbent upon pathologists to make a careful study of all that can be seen in the microscopic examination of fresh, macerated, and preserved cancerous material, and whatever else may be the outcome of such studies, they will have furthered our knowledge of cellular degenerations and metamorphoses. Unless there are those present who on the basis of such study are prepared to discuss Dr. Gaylord's findings, it does not seem to me worth while to discuss them in detail.

Dr. Gaylord has presented an instance of multiple nodules in the lungs of an adeno-carcinomatous nature following the intravenous injection of cancerous ascitic fluid. With this exception and one or two more doubtful cases his experimental results, so far as the reproduction of malignant tumors is concerned, are, like those of other investigators in the same line, negative.

May 6, 1901.

The meeting was called to order by the President, Dr. Welch.

A Case of Pseudo-parasitism. DR. STILES.

Exhibition of Medical Cases. A Case of Charcot's Joints involving both Knees. DR. FUTCHER.

This colored man is 68 years of age and manifested the first symptoms of tabes seven years ago in the form of lightning pains in both lower extremities. Two years later the right knee suddenly became swollen and inside of two weeks he noticed that the knee would give laterally whenever he attempted to bear his weight on it. Two weeks after the onset of the symptoms in the right knee the left knee became similarly involved. There was no pain at the onset, and there has been none throughout its course. In November, 1900, the right knee suppurated and was opened. The knee-joints, as you observe, now show the most marked deformity. The tibia on both sides is dislocated outwards on the femur, and there is very extensive lateral motion with hyper-extension of both knee-joints. The condition presented is that of Charcot's joint complicating tabes dorsalis.

Charcot first described the joint affections associated with tabes in 1868. The joints involved are usually the large ones and rarely, with the exception of those of the feet, are the small joints of the body affected. The joints of the lower extremities are more frequently affected than those of the upper. Chipault collected 268 cases of tabetic arthropathies, of which 120 were in the knee and 57 in hip joints. The character of the changes in the joints varies greatly with the type of the joints, as to whether they are ball-and-socket or hinge joints. In the first, such as the shoulder and hip, atrophy is more likely to occur than hypertrophy. In the knee, hypertrophic are more common than atrophic changes, and consequently there is more deformity. This complication of tabes often occurs comparatively early in the disease, and some observers say it may be the first symptom to attract

the patient's attention. On the other hand some cases may come on very late in the affection.

The tropho-neuroses in tabes dorsalis are varied and divided by some into the osteopathies, arthropathies and osteo-arthropathies. To the osteopathies belong the spontaneous fractures in the long bones. The arthropathies include the cases with Charcot's joints. The osteo-arthropathies comprise those cases where the joints and bones are involved together, and in this group belong the vertebral lesions with kyphosis, as well as those cases of tabetic feet where the foot is foreshortened because of dislocation of the metatarsus backwards on the tarsus.

In the hypertrophic form of Charcot's joints the examination will show destruction of the cartilages with hypertrophy of the synovial fringes and thickening of the ends of the bone with rarefaction and consequent softening of the bone tissue. Occasionally the cartilages may be eburnated, but this is uncommon.

As to the treatment of tabetic joints there is very little that can be done to give permanent relief or improvement. In recent years an effort has been made to secure relief by excising the joints. We have had one case here in which excision was performed two years ago. The upper end of the tibia and the lower end of the femur were excised and the two extremities coapted, but at the last report union had not occurred. An interesting point was that the patient did not require an anæsthetic. He lay on the table perfectly conscious of what was going on. The bones were sawn through and the periarticular tissue removed without his experiencing the slightest pain. In the case before you the patient did not suffer any pain when the right knee-joint was opened.

Protozoic and Blastomycetic Dermatitis, with Lantern-slide Demonstrations and Exhibition of a Case. DR. GILCHRIST.

DISCUSSION.

DR. STILES stated that when the cases first came up specimens of the parasites were submitted to prominent botanists, who concluded that they did not belong to the plant kingdom. After this opinion had been expressed by several well-known mycologists, he had reluctantly adopted it, and because of the resemblance of the parasite to *Coccidium*, and because of its method of reproduction, he had placed it in the sporozoa. He had advised Doctor Gilchrist to classify it temporarily in the microsporidia, chiefly because he did not see in what other group it could be placed, and not because he felt positive that it was a true microsporidium. The case at hand was an excellent example of the difficulty which frequently arises in determining whether a given organism is an animal or a plant.

May 20, 1901.

The meeting was called to order by the President, Dr. Welch.

Exhibition of Medical Cases. DR. OSLER.

CASE 1.—This patient was admitted May 16, complain-

ing of stomach trouble. He is a laborer, aged 37--had jaundice when seven years old, which lasted about a year, and which is a point of interest in his history. Since then he noticed a yellow cast of the eyes whenever he felt badly, though we could not get a distinct history from him of permanent slight jaundice. There is no history of any acute illness of any moment. He has been a heavy eater and a drinker of beer from his sixteenth year, but has not used whisky. There is a suggestive history of lues.

The onset of his illness occurred May 7 with cramp-like pains on the right side, just under the ribs. He worked all that day and obtained relief from his pain by forced vomiting. A slight pain continued for several days but did not prevent his working. He lost ten or twelve pounds in weight before admission. He has had no fever and is a robust, rather healthy looking individual. In this light you do not especially notice the jaundice, but it is one of those instances where, having seen him in daylight and having his color fixed upon your mind, you can see that he is a little jaundiced. The point of special interest is the abdomen. You can readily see a slight fullness in the left umbilical region, and as he draws a deep breath you notice a distinct shadow. There is a marked difference between the infra-costal grooves on the two sides. On palpation, there is in the left hypochondriac region and extending into the umbilical and epigastric regions a solid, firm tumor mass, the edge of which can be readily felt below and to the right. This mass is rounded, firm, very mobile and the hand can be passed behind it pushing it forward. Its edge is felt to be distinctly notched. There is no question at all that it is an enlarged spleen. It is a spleen of moderate size and not one of those that reaches almost to Poupart's ligament.

On examination the liver edge can not be felt on palpation at first, but on deep inspiration the edge descends and can be felt at the time of extreme inspiration. On percussion you notice a small area of hepatic flatness, not more than two fingers' breadth, and there is no ascites. He feels well and the jaundice and pain, which latter is better now, are the only two features of which he complains. His blood does not show any marked anemia; there is no leucocytosis and the hæmoglobin is 70%.

The interesting features are the presence of a very large spleen, with a very small liver, and jaundice without anemia. The case belongs to those interesting groups of which we have had a number of cases lately, illustrating the association of enlarged spleen with cirrhosis of the liver. There are several different conditions in which we may have splenomegaly with cirrhosis of the liver.

First, it is the rule in cirrhosis of the liver to have a big spleen and in a few rare instances in ordinary cirrhosis from alcohol the spleen reaches an enormous size. Some of you may recall a case we had in the hospital two years ago which we thought at first was very probably one of primary disease of the spleen, but which was shown later to be an enlarged spleen associated with a diseased liver.

Second, in all cases of hypertrophic cirrhosis, particu-

larly those of the so-called Hanot type, the form that occurs in young children and persons without an alcoholic history, there is no ascites, but a permanent slight jaundice. Sometimes there is a very large spleen in these cases, a spleen equalling in size, or even exceeding the size of the liver. Many of you recall the two brothers (White) who were here for several years under observation, both having very large spleens. There is a good series of pictures in the last number of Guy's Hospital report with an article by Dr. Taylor particularly illustrating this form.

Third, there is an interesting group of cases, which we have been studying carefully during the last few years, in which there is a primary enlargement of the spleen associated with slight, but characteristic anæmia. Some of these cases show no anemia, but progressive enlargement of the spleen, sometimes without any other symptoms whatever. Such a patient may come, as some of our cases have, not complaining of the spleen, or of abdominal pain, but with hemorrhage from the stomach. In a certain number of those cases the liver has been atrophied. Banti, of Italy, has studied a number of them and the condition has been called Banti's disease. The anæmia is of the chlorotic type and as a late sequence there is cirrhosis of the liver. We have had two such cases, one of which was operated upon by Dr. Cushing for removal of the spleen which had been enlarged for eight or ten years. In that case there was a well marked ordinary cirrhosis with anemia. The second case was operated upon by Dr. Halsted a few weeks ago and here the liver was cirrhotic and the condition had lasted for six or eight years.

The case before us I think may be called a primitive splenomegaly with cirrhosis of the liver. He has been a beer drinker it is true, but you rarely get a marked cirrhosis in such people at this time of life and he has not the facies of ordinary cirrhosis.

CASE 2.—I wish to show this case for just one point. It is a case of scurvy with an unusual condition of the skin of the legs. In a few instances of scurvy there are very extensive subcutaneous hemorrhages particularly about the thigh and knees, and they may be so extensive and diffuse that the leg is in a sclerotic or scleremie condition. We have had one case in which the patient could not straighten his legs when he attempted to walk but simply shuffled them along. This man came in with swollen gums, with hemorrhages, and an enlarged knee. Aspiration showed bloody fluid in the knee-joint. The swelling is such that you can not pick up the skin at all on the hemorrhagic side. The condition is known as scorbutic scleroderma. The patient has only been in this country about a year, working at Locust Point, and has eaten practically nothing but meat and bread during that time.

DR. WELCH.—What is the value of treatment by extirpation of the spleen in Banti's disease?

DR. OSLER.—In Dr. Cushing's case, where the condition had lasted for eight or ten years, the spleen was removed, with complete recovery, and the patient has been well now nearly two years. In the second case that was operated upon,

the patient did very well for more than a week and then had a recurrence of the hemorrhages and died with a very profuse hemorrhage, which the post-mortem showed was from an œsophageal varix. The third case operated upon a few weeks ago by Dr. Halsted had a very large spleen with hemorrhages recurring for six years, and on four or five occasions the patient nearly bled to death. At the operation the splenic veins and arteries had been tied but in attempting to remove the adhesions between the spleen and the diaphragm an uncontrollable hemorrhage occurred and the patient died.

Drainage of the Bladder and Cystoscopic Examinations. DR. KELLY.

Dr. Kelly spoke of drainage in bad cases of cystitis. Here attempts to wash out will be cut short on account of the pain. Dr. Kelly treats such cases by placing the patient in the knee-breast position and letting air into the bladder through the cystoscope. He then thrusts in a narrow-bladed, specially made knife, set at an angle with the handle, and draws it downward towards the urethra, leaving a free opening into the bladder for escape of urine. Dr. Kelly urged the importance of making topical examination of the bladder before commencing treatment in cases of apparent cystitis. He had had cases which had been treated elsewhere for a length of time for cystitis, when on using the cystoscope a stone was seen, and in its removal the symptoms disappeared. He spoke also of peculiar cases of pregnancy which he does not understand. One part of the uterus softens down and the rest remains rigid; the softened part may bulge. In his case it was mostly towards the patient's right. The patient was the wife of a physician from Iowa. He was advised to let it alone and returned home, where his wife had a normal labor. In another case, the wife of an army surgeon, the abdomen was opened and the right upper horn of the uterus found to be softened. The patient later aborted per vias naturales. In a third case exactly the same condition was found. Dr. Kelly would call it "apical pregnancy," and it is liable to be mistaken for extrauterine pregnancy.

Observations upon Smallpox. DR. OTLEY J. PORTER, of Columbia, Tenn.

Dr. Porter described an epidemic that has recently prevailed in that section of Tennessee in which he lives. For a time the diagnosis was in dispute, some regarding it as chicken-pox, others as a new sort of eruption, "the bumps," and a few diagnosing true smallpox. Meanwhile, in the uncertainty there was no efficient action or isolation, and the disease spread until there were 1000 cases. Dr. Porter exhibited casts of the eruption and threw pictures on the screen, showing that the disease differed in no way from the smallpox of the text-books, there being cases of hemorrhagic, confluent, semi-confluent and discrete smallpox, as in other epidemics. The mortality also was the same, all the hemorrhagic cases (5 or 6) dying; 40 per cent of the confluent, and 10 to 15 per cent of the discrete. Old persons over 75,

pregnant women and infants under 12 months are usually exempted from the need of vaccination, but none need it more than these persons. In the 1000 cases there were some 15 of the disease in the fetus in utero, several of which Dr. Porter had himself delivered.

DISCUSSION.

DR. FULTON.—It is very fortunate for the State of Maryland that a dispute about the diagnosis of this disease has not arisen here. I doubt whether anybody would have made and defended the true diagnosis in the way it has been done in Tennessee. Some of the big wigs in that State were on the side of chicken-pox in that controversy. Before engaging in a controversy with a man who collects evidence so carefully and presents it so vividly, one must be very sure that he is right, for there are only two alternatives, to be right or to run. In Tennessee the big wigs ran, as wise men should in such a predicament.

It is not surprising that errors of diagnosis have been frequent in the history of the smallpox epidemic now prevailing in the United States. The disease itself departs widely from the text-book descriptions, though not more widely than typhoid fever does; and these variations are no less manifest in its epidemic characteristics than in the individual cases. The medical student of to-day has no chance to observe the disease, and has therefore no mental picture of the disease other than that gained from the text-books. Comparatively few physicians under 50 have seen the disease, while the older men remember the disease by the more impressive characteristics of its appearance years ago.

Besides, there are fundamental reasons why the diagnosis of the eruptive fevers should sometimes be difficult. Knowing as we all do in what varying degrees the animal body reacts to the infections, it seems strange that medical men expect reactions to the same organism to be always similar in kind. Every eruptive fever is known by its peculiar dermatitis. Fortunately the appearances of the skin in measles, scarlet-fever, chicken-pox, and smallpox are usually characteristic enough, in conjunction with other data, to lead to correct diagnosis. Chicken-pox and smallpox are, however, strikingly alike at times, and in the present epidemic this is particularly true. As one's experience grows, one approaches the problem of diagnosis in each new isolated case with increasing diffidence. Watching the whole evolution of the lesion, one should not go astray, but this deliberation about diagnosis does not satisfy the demands of public safety, nor the clamor of private interests, when smallpox is suspected. It will be remembered that Hebra taught that variola and varicella were one disease, and some of his pupils still hold that doctrine.

The signs of the times are but slightly hopeful that we shall soon have identified the contagium vivum of smallpox, and the controversies about diagnosis will not wholly disappear until that comes about. Two recent communications upon this subject are of interest. M. Funck, of Brussels, describes what he calls the sporidium vaccinale, which he

thinks he recognizes in three stages. 1st, small, spherical, highly refracting bodies of a green color, having slow movements, and varying in size from 2 to 10 micromillimeters; 2nd, collections of smaller refracting spheres enclosed in a sort of capsule; and 3d, morula masses 25 to 30 micromillimeters in size, which he thinks are spore cysts. He studies the sporidium by the hanging drop method, in a warm, moist chamber. The sporidia, he says, attach themselves to the cover-slip, while the other elements fall toward the apex of the drop. Funck also claims to cultivate the organism. He spreads vaccine lymph on ordinary agar plates, which are inoculated for 24 hours. The sporoblasts are, after incubation, recognized under a low power. He picks these out with a platinum needle hammered into a sort of spatula. With this tool he transfers the sporoblasts to bouillon, and the resulting emulsion, he says, produces typical vaccinia when inoculated into a calf. He gets the same organism from the lesions of variola.

A second and more hopeful communication is that of Copeman, who described in 1896 an organism that he was able to cultivate from vaccine lymph, using the hen's egg as a medium. His experiments failed frequently, and recently he has come to the conclusion that his failures were due to his working with eggs that were not fertile. He insures this now by incubating his eggs for a short time, using only those which prove fertile. He also used the collodion capsule method of inoculation. Bouillon cultures of glycerinated vaccine enclosed in collodion capsules are placed in the peritoneal cavity of the dog or the rabbit, and after 14 days are removed, when stained films show zooglea masses, made up apparently of spores. With the bouillon Copeman produces vaccinia in the calf. Bouillon cultures in collodion sacs, similarly inoculated, are put in plain bouillon test tubes and kept in the thermostat for the same period. The contents of these capsules, used as controls, do not produce vaccinia in the calf.

I should like to use the lantern for a few illustrations of smallpox cases recently observed in Maryland (Illustrations).

DR. SMITH, Minneapolis.—I would like to speak of the results of the epidemic in our city. We have been passing through an epidemic of this disease and this exhibition of Dr. Porter's has been very interesting to me because one of our physicians has been doing similar work. His casts, however, were made of wax and were colored. They were presented to the University of Minnesota Medical Department and are being used now to show the students the picture of a disease they will not see in life.

We met with considerable difficulty at first in the diagnosis and the city had fifty cases before the health commissioner would recognize it. If it had not been for the very efficient work of Dr. Bracken, the secretary of our State Board of Health, the epidemic would have been much more dangerous than it was. He worked night and day to suppress it and at times quarantined whole sections of the State. We could trace the disease to two women who came to the city infected. One of the peculiarities noticed at first was

the appearance of a bracelet around the wrists and of hard nodules in the palm of the hands. We knew those were not chicken-pox cases, and wherever we found itching or eruption on the hands, we quarantined that person.

As to the question of vaccination

Closing Discussion of Dr. Porter's paper.

DR. PORTER.—In regard to the remark that it is left for the future to say whether we have had a modified form of smallpox in this epidemic, I think one point may be mentioned to prove that this was not a modified form. The different types of the disease were interchangeable even in the same family—for instance in one family that I knew of, the daughter had a mild attack of the discrete form. The mother, who refused vaccination, contracted the disease and died of the malignant hemorrhagic type, while her husband developed the ordinary confluent form. Assuming that we have a modified form, or an attenuated microorganism, it is difficult to understand these cases.

In regard to the vaccination of cases that have recovered from smallpox, I made that test in twenty-five cases and did not get a take in any instance. I got two septic sores, but they were not the typical vaccine sores. Other gentlemen made the same experiments, and as far as I know all failed, but of course it is not impossible that it might happen.

Adjournment.

June 3, 1901.

Fibrinous Bronchitis. DR. BETTMANN.

(Paper to appear in *The American Journal of the Medical Sciences*).

Maggie Scott, colored, female, married, age 22, mother of two children, labors normal, no history of tuberculosis; menstrual history normal. The patient was admitted to the Maternity Ward of the Johns Hopkins Hospital August 20, 1900, with the following history: At various times throughout the past six years she has suffered from attacks of cough, pain, respiratory distress, and profuse expectoration of branching casts usually in the autumn. Although she has gradually emaciated during the past three years she has been well during the intervals between the attacks, which have had no relation to her pregnancies.

Her present attacks occurred thirteen days after normal labor, and were characterized by a slight bronchitis, extreme respiratory distress, a rise of temperature to 102°, and a cough which was relieved by the expectoration of casts. She had two similar attacks subsequently with an interval of eleven days between them. She left the hospital in spite of the protests of her physician four days after her last attack, when she still had some slight evening temperature (rarely 101°). She remained in Baltimore three weeks and had similar attacks during that period, and two weeks later she died in Virginia. No data as to the cause of death were obtainable. It should be added that the possibility of a puerperal infection was excluded by the absence of local signs and the general good condition of the patient. There was intense dyspnoea and severe coughing during the attacks, with pain

in the left side of the chest. There were present râles of all types, impaired resonance, and a small area of tubular breathing in the right lower lobe during the first attack. In the intervals between the first and second attacks an area of impaired resonance and impaired breath sounds were detected in the left axillary region. There was no leucocytosis; differential count normal; no albumin in the urine.

CASTS.—During the two most severe attacks the patient coughed up two casts 10 cm. long which showed branching down to the 10th or 12th degree; other smaller casts were coughed up in the interval. These, on cross section, showed an outer laminated "skin," inclosing separate whirls and complete cylinders. Air vesicles were seen throughout the casts. Little intumescencia were seen at the ends of the finer branchings. The use of Weigert's fibrin stain showed surprisingly little fibrin distributed in the outer layer of the casts. Hematoxylin and cosin stains showed mucin and a substance taking the eosin stain deeply but not staining with the Weigert stain. This substance, from its staining reactions, did not seem to be mucin or fibrin but contained the fibrillae that retained the fibrin stain. The cells are mostly small mononuclear leucocytes; a few eosinophiles are present; no polynuclears. There were no Charcot-Leyden crystals. Throughout the casts were irregularly round bodies, the size of a red blood corpuscle, staining with the Weigert stain, with the tubercle stain and with eosin (cosin methyl-blue method). These apparently had a double contoured shell, from which, in places, an inner granular and vacuolated protoplasm seemed to have shrunk away. They reminded one of the blastomyces which Gilchrist has described in dermatitis. Bacteriologically the casts showed staphylococci and streptococci on the outer side of the outside layer. Occasional organisms were seen in the inner portion of the cast. Cultures taken under antiseptic precautions from the interior of the cast showed the presence of staphylococcus aureus, streptococcus pyogenes. There were no pneumococci and no diphtheria bacilli.

An analysis was then given of Lebert's paper in *Deutsches Arch. klin. Med.*, 1869. To this was added an analysis of all cases of fibrinous bronchitis in French, English and German literature since 1869.

The author grouped the cases reviewed into 9 groups for purposes of description: I. and II. Chronic and acute cases with expectoration of branching casts, 27 and 15 cases respectively. III. Cases in which branching casts were not expectorated but were found at autopsy, 6. IV. Cases in which the casts expectorated showed no dichotomous branchings, 11. V. and VI. Expectoration of branching casts in the course of organic heart disease and pulmonary tuberculosis, 10 and 14 cases respectively. VII. Expectoration of small casts often not branching in asthma, 5 cases. VIII. Formation of casts in bronchi following thoracentesis, 4 cases. IX. Poorly reported cases, 6.

The author demonstrated sections of casts in various stains under the microscope as well as hardened specimens.

The Life History of Drepanidium. HERBERT E. DURHAM and the late WALTER MYERS. (Liverpool Yellow Fever Commission.)

The smaller kind of toad found at Pará, Brazil, was found to be infested by endoglobular blood parasites. In all the specimens examined two forms of parasite were found: (1) with highly refractile protoplasm and granules, and of more or less irregular shape, and (2) with pale protoplasm and elongate and fusiform in shape. The former correspond to the "Dactylosoma" described by Labbé (*Archives de Zoologie Expérimentale* —? 1895 —) and the latter to the form known as *Drepanidium*; both of these two forms were always present, though in varying proportion. The highly refractile form, when fully developed, is of an irregular amoeboid shape or somewhat like a bent blunt club; segmentation or sporulating forms in a fan-shaped arrangement are occasionally met with, these often appeared to be referable to a tripartite division whereby each of three lobes gives origin to three small bodies. We had no evidence that the adult refractile forms ever leave the host-corpuscle, the nucleus of which, however, is dislocated. The *pale form* lies alongside the nucleus of the corpuscle, which is not displaced. When mature it leaves the corpuscle in specimens of shed living blood, and swims freely with its narrower extremity forwards. We are doubtful whether these forms ever leave the corpuscle *WITHIN* the body of the toad, for in specimens of blood which had been fixed with weakly sublimated saline solution and centrifugalized, no free forms could be found; thereby contrasting with similar specimens made without the fixing agent in which hardly a single endoglobular individual could be found. The multiplication of these forms takes place chiefly in the liver (less in the spleen, and less still in sternal marrow), where cysts about 10 μ in diameter containing immature pale forms may be found in great abundance. The mode of entry of these into individual red blood corpuscles was not observed.

The toads were mostly infested by a species of tick: Examination of the contents of ticks showed a graduated series of cysts up to about 60 μ in diameter. The cysts consist of a thin hyaline membrane (as seen in ruptured or empty specimens) and fragmented protoplasmic masses lying within it; usually also there are two or three larger protoplasmic masses attached by bridles to the periphery. The small fragmented masses correspond in appearance to small, actively motile amoeboid bodies, found in the contents of the tick and the plasma and corpuscles of the toad. Conditions suggestive of conjugation of the free drepanidia have been seen in the tick, where their movements are more rapid than in plain films of toad's blood. The examination of cattle- and dog-ticks failed to reveal cysts similar to those above mentioned, and we presumed that these were a stage of development of the blood parasites of the toad. On this conception the cycle may be compared to that of the malaria parasite in its development in circulating blood, organs (marrow and spleen) and in the anopheles group of gnats.

Asexual cycle within blood corpuscle of toad ("Dactylosoma").

Sexual cycle multiplication in organs (liver) of toad: leaves blood corpuscles ("Drepanidium") within tick: probable conjugation resulting in formation of cysts: which give rise to minute amœboid spores.

Owing to the length of time of attachment of the tick many stages are seen contemporaneously. From lack of material it was not possible to make infection experiments upon uninfected toads.

NOTES ON NEW BOOKS.

The Hygiene of Transmissible Diseases: their Causation, Modes of Dissemination and Methods of Prevention. By A. C. ABBOTT, M. D., Professor of Hygiene and Bacteriology, University of Pennsylvania. Third Edition. Revised and Enlarged. Octavo, 351 pages, with numerous illustrations. (Philadelphia and London: W. B. Saunders & Company. Cloth, \$2.50 net.)

A review of the first edition of this excellent work appeared in the BULLETIN for March 1900. Since that time investigations upon the modes of dissemination of certain of the specific infections have been conspicuously active, and through them much new light has been shed upon the transmission of diseases and many novel suggestions have been made; especially is this the case with regard to the roles of insects and rodents as disseminating factors. Wherever practicable, these views have been embodied and discussed in the present edition. The resume of our latest knowledge of malarial fever is especially good. In the treatment of the subject one feels that the author has been hampered by what he had previously written, and that the new and the old are not wholly harmonious. It is to be hoped that in the next edition the state of our knowledge of malarial disorders may be so complete as to justify the rewriting of the whole section. The sections on Yellow Fever, Plague and Dysentery are most valuable. The book is in every way more satisfactory than was the first edition.

We notice one or two typographical errors, as e. g., on page 214 *Koplic* twice for *Koplik*, page 270 *Clements* for *Clement*, and page 216 "periodic recurrence or paroxysms" for of paroxysms.

Golden Rules of Hygiene. By F. J. WALDO, M. A., M. D. (Cantab.), D. P. H., Barrister-at-Law. Golden Rule Series No. X. (Bristol: John Wright & Co.)

This concise little book gives very sensible suggestions as to Air, Water, Disposal of Refuse, Food and Infectious Diseases. The rules are well arranged and easy of reference.

Essentials of Refraction and of Diseases of the Eye. By EDWARD JACKSON, A. M., M. D., Emeritus Professor of Diseases of the Eye in the Philadelphia Polyclinic. Third Edition, Revised and Enlarged. 12mo, 261 pages, 82 illustrations. (Philadelphia and London: W. B. Saunders & Co., 1901. Cloth, \$1.00 net.)

In this edition the work has been carefully revised and very much enlarged, the contents being more complete and more symmetrical than was possible in the earlier editions. The injuries of the eye by traumatism, and the ocular symptoms and lesions of general diseases have now been given a consideration proportioned to the great importance they assume in the work of the general practitioner. There has been added

also an account of the application of the tests of vision required in the army, navy and railway service.

This work has long since proved its usefulness to the beginner in ophthalmic work, to the student, and to the busy practitioner. The entire ground is covered, and the points that most need careful elucidation are made clear and easy.

Burdett's Hospitals and Charities, 1901. Being the Year Book of Philanthropy and the Hospital Annual. By Sir HENRY BURDETT, K. C. B. (London: The Scientific Press (Limited), 28 & 29 Southampton Street, Strand, W. C.; New York: Charles C. Scribner's Sons.)

We are glad to welcome the twelfth year of the above publication. The manual is an invaluable aid to all persons who have to do with charitable work, and the author has done more to systematize hospital methods in this country and in Europe than any other single person. The volume contains much interesting reading, some of which commends itself especially to one who lives in America and is familiar with the freeness and liberality of the hospitals of the United States. It is interesting to notice that there are seven hospitals in London where the patients are required to supply their own tea, sugar, and butter; thirty-three hospitals where patients must supply a change of bed-linen; and nineteen hospitals where patients are under the necessity of paying extra for laundry work. At twenty-two hospitals patients are required to provide more or less of the following articles: towels, slippers, knife, fork and spoon, brush and comb, soap, plate, cup and saucer; but it is gratifying to know that there are twenty-two hospitals where patients are not required to furnish anything. In the Provinces the number of hospitals requiring miscellaneous articles to be supplied is very great. It would seem in fact from reading the list, that poor patients are obliged to supply an almost impossible number of requisites. The author's very commendable reasons for furnishing the above list are: "First of all, it is desirable, in the best interests of the institutions and of those whom they treat, that the in-patients should be required to provide nothing. Discipline, cleanliness, and due regard to the circumstances of the poor, all demand the abolition of the old-fashioned practice of allowing patients to provide even personal linen, much less to permit them to defray the cost of their own washing. Secondly, any one who has a knowledge of hospital accounts will readily recognize the considerable reduction which there ought to be in the cost per bed, in the case of hospitals which require the in-patients to supply themselves with linen and groceries."

The book is admirably printed and well arranged. It is surprising that it has been possible to secure so much information respecting American hospitals and training schools for nurses.

Practical Surgery: A work for the General Practitioner. By NICHOLAS SENN, M. D., Ph. D., LL. D., Professor of Surgery, Rush Medical College, Chicago. Handsome octavo volume of 1133 pages, with 650 illustrations, many in colors. (Philadelphia and London: W. B. Saunders & Co., 1901. Cloth, \$6.00 net.)

Like all other practical works representing the surgical methods of an operator who has had many years' experience this book of Professor Senn is destined to be of great service to the profession at large. It does not claim to be a systematic treatise on surgery, but simply a statement of those things which the every-day practitioner is likely to meet with in the practice of surgery, either in the city or country. It contains an account of Professor Senn's experience with gun-shot wounds and injuries in the Spanish war and also in the

Turkish war. His treatment of gun-shot wounds is eminently sensible. He speaks of the necessity of a complete immobilization of the injured parts and of perfect antiseptic work in connection with all first dressings. It is gratifying to know that by means of first aid packages and other modern devices, the dreadful aspects of military surgery a hundred years ago are completely changed. He deplores the failure of laparotomy performed on the field for gun-shot wounds of the intestines, although it is not strange that such surgery should be ineffectual.

The chapters on fracture are also extremely interesting, especially his treatment of fractures of the hip. We are glad to notice that he condemns absolutely the ambulatory treatment of compound fractures.

At first glance it might seem strange that he does not refer to gall-bladder operations, operations for the relief of breast cancer and operations for the removal of the Gessarian ganglion but it should *not* be forgotten that the treatise is for the general practitioner and surgeon rather than for the surgeon who is in a position to do special operations. The operations alluded to require a degree of expert knowledge which can only be acquired after very long practice. Hence, wherever practicable, it would seem extremely judicious to reserve such specialized operations for specialists in private or general hospitals who do them frequently.

The book is beautifully printed and well gotten up. A few typographical errors are to be noticed, especially in the names of individuals.

An interesting feature of the book is the attempt to emphasize important points by the use of italics. Although one is generally opposed to the wholesale use of italics in journal articles, in the present instance their employment seems judicious and helpful to the general reader.

Principles of Surgery: By N. SENN, M. D., Ph. D., LL. D., Professor of Surgery in Rush Medical College in affiliation with the University of Chicago; Professional Lecturer on Military Surgery in the University of Chicago; Attending Surgeon to the Presbyterian Hospital; Surgeon-in-Chief to St. Joseph's Hospital; Surgeon-General of Illinois; late Lieutenant-Colonel of United States Volunteers and Chief of the Operating Staff with the Army in the Field during the Spanish-American War. Third Edition Thoroughly Revised. With 230 wood engravings, half tones and Colored illustrations., (*Philadelphia and Chicago: F. A. Davis Company, Publishers, 1901.*)

This work is a pioneer in its class in this country. Like the other writings which have come to us from the author, it shows a complete mastery of the methods of imparting interest to difficult subjects.

The title might just as well have been "Surgical Pathology" for this is the main feature of the work, which one might infer from the title "Principles of Surgery." Practical details in treatment are not wanting by any means. They are terse as a rule and where diagrams can take the place of wordy details they are inserted. The illustrations are numerous and clear, the skiagraphs making a valuable addition to a work on practical surgery.

Usually the author takes the broadest scientific view of the matter and gives us the most recent knowledge on all subjects with which he deals. After describing erysipelas at some length he states very positively "the streptococcus of erysipelas never produces suppuration." It is on bone tuberculosis that his clearing out is of particular value. He is liberal in his views, not holding us fast to any one line of thought unless there is unmistakable scientific proof for his way of thinking. Owing to the arrangement of the subjects it is

difficult to locate the practical surgical details until after having read the entire book.

Some surgical points on bone surgery are to be found under osteomyelitis, others under tuberculosis of bone or joints; again others under abscess.

The treatment of paronychia and tendo-vaginitis is described under suppuration. Under healing of wounds is given what he has to say on technique and sutures. After exhorting to absolute asepsis, the author deals with haemostasis, suturing and physiological rest. He deals with regeneration of different tissues, describes tenorrhaphy, nerve suture and healing of wounds of organs.

Degeneration is as thoroughly described as in text-books on pathology.

As inflammation is divided into acute and chronic forms, so is suppuration described as acute and chronic.

The pyogenic organisms and all other microorganisms known to the surgeon are thoroughly described along with something of the history of their discovery.

There are many little points valuable to the practicing physician which are only found after careful reading. The significance of pain is described under inflammation. It is made of diagnostic value in periostitis and syphilitic bone disease.

Inflammation, one of the most difficult subjects to treat, is very nicely dealt with from both the scientific and practical sides. Senn states that "inflammation is always caused by the presence of one or more kinds of pathogenic microbes" and must be sharply distinguished from the regenerative processes. The treatment of the subject of ulceration is clearer and more practical than in most text-books on surgery. Senn allows for varying local and general conditions, tissues involved and microorganisms present in the classification of ulcers. He thinks that all ulcers are caused and maintained by pathogenic microorganisms.

The treatment of the subject "tuberculosis" is excellent. It is most comprehensive and, considering the limits of the book, it is very thorough. One of the chief characteristics of the book is the direct manner in which the lessons are taught.

Senn's book is a natural outgrowth of the times. It comes at a transitional period for students who are learning to combine the science and practice of medicine more intelligently than in former days. It is a book which should be at the hand of every surgeon.

S. M. C.

Atlas of the Nervous System, including an Epitome of the Anatomy, Pathology, and Treatment. By Dr. CHRISTFRIED JAKOB. With a preface by Prof. AD. V. STRUMPELL, Edited by EDWARD D. FISHER, M. D. With 112 Colored Lithographic Figures and 139 other Illustrations, many of them in Colors. (*Philadelphia and London: W. B. Saunders & Co., 1901.*)

The present Atlas is designed to give students and physicians an adequate conception of the relations of various parts of the nervous system to each other. The illustrations are unusually good and some of them are extremely graphic. Those relating especially to the cortex of the brain are works of art. The principal value of the book, of course, is in its appeal to the eye, and the endeavor which it successfully makes to illustrate adequately the subject represented. The portion of the book which relates to general pathology and treatment is rather disappointing, because of the great brevity which is necessary from an effort to compress the material into the space allowed. The book, however, is creditable in every respect. It is well printed and attractively bound.

A System of Physiologic Therapeutics. A practical exposition of the methods, other than drug-giving, useful in the treatment of the sick. Edited by SOLOMON SOLIS COHEN, A. M., M. D., Professor of Medicine in the Philadelphia Polyclinic, etc. Vol. II. Electrotherapy. By GEORGE W. JACOBY, M. D., Consulting Neurologist to the German Hospital, New York City, etc. In two Books, Book II: Diagnosis, Therapeutics. Illustrated. (*Published by P. Blakiston's Son & Co., 1012 Walnut St., Philadelphia, Pa. Price eleven volumes, \$22 net.*)

This volume, like all other honestly written books on electrotherapy, is in some respects disappointing. The gist of it seems to be that electricity, after its use as a diagnostic agent is eliminated, is mainly serviceable by way of mental suggestion and for its psychic effect. The sections of the work which treat of electrophysiology and electropathology and of electrodiagnosis and electropagnosis, seem especially valuable, and are worthy of great praise for their clearness and conciseness. Methods of examination are carefully given and charts and diagrams render very clear the proper points for the electrization of muscles and groups of muscles in every part of the body.

When we come to the sections on electrotherapy we learn that electricity acts through a combination of exciting electrotonic, chemical (and electrolytic) cataphoric and psychic or suggestive actions, and that "how great an effect is to be ascribed to each individual action has not been and cannot be demonstrated" . . . "That however, psychic influence does form a very large part of the therapeutically beneficial action of electricity is undoubted, because the channels through which it may act are manifold." All the other effects may "abide" but the greatest of these is the psychic or suggestive effect of electricity. This confession helps to explain why electricity has invariably been the right hand of the quack and charlatan, but it also tends to discourage the student of medicine who has lived in hope that, sooner or later, order in electrotherapeutics would emerge from chaos, and electricity as a remedy

for the cure of disease, would take a fixed and dependable place in the medical armamentarium.

The book, as a whole, is a discriminating one and must do good by placing electrotherapy upon a less pretentious and more scientific basis. It should be diligently studied by all who use electricity as a therapeutic agent.

The American Illustrated Medical Dictionary. A new and complete Dictionary of the terms used in Medicine, Surgery, Dentistry, Pharmacy, Chemistry and Kindred Branches, with their pronunciation, derivation and definition, including much collateral information of an encyclopedic character. By W. A. NEWMAN DORLAND, A. M., M. D., Fellow American Academy of Medicine. With numerous illustrations and 24 colored plates. (*Philadelphia and London: W. B. Saunders & Company, 1900.*)

In shape, size, binding and typography this volume is all that can be desired for convenience and handy reference. The print is compact and the sizes of type are so well adjusted to each other, the page does not fatigue the eye. The binding in limp leather renders the book easy to handle. The definitions in some instances are open to criticism, e. g. "Paranoia, Mental aberration or eccentricity with perversion of the will, in pronounced cases it is a form of insanity." As a matter of fact paranoia is a form of mental disease and characterized by systematized delusions arising primarily, that is without antecedent excitement or depression. The definition of *B. aërogenes Capsulatus* is also faulty, "a pathogenic form from the blood-vessels in a case of thoracic aneurism." Whatever may have been the disease in which this bacillus was first found it has been met with since in many other situations besides the blood of a thoracic aneurism.

There are also some omissions, as e. g., Dementia precox cannot be found under the head of dementia.

The illustrations are good and many of them give valuable aid to the text. The book can be commended as convenient and useful.

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CARCINOMA OF THE MALE BREAST.*

By LOUIS M. WARFIELD, M. D.,

House Medical Officer, The Johns Hopkins Hospital.

Although carcinoma of the male breast is not a very uncommon occurrence, it is of sufficient rarity to justify a few remarks on the subject with a review of the cases published in the literature in the past ten years.

Naturally a number of explanations have been offered to account for the relative rarity of this condition in men as compared with women, and the one most generally accepted is that it is due to the inherent difference in the function of the gland in the two sexes. In the first place the female mamma is more apt to be injured for obvious reasons, and in the second place it passes through a series of changes tending to make it susceptible to new growths of all kinds. Up to the time of puberty the gland is quite similar in the two sexes, but from that time the course of one is, if not regressive, at least stationary, with a poor blood supply, while in that of the other there is growth of all the ducts and acini with consequent greater vascularity. Then, too, at every pregnancy the breast proper proliferates, the gland functions during lactation, and after the child is weaned the mamma goes through a series of regressive changes, becoming more and more fibrous, until after the menopause, very little of the true gland tissue remains. However, carcinoma of the breast in both sexes has its origin in the gland epithelium, whatever view one holds as to its etiology, and it is a well known fact

that a growth may exist as a small, painless nodule for years, and suddenly take on malignant characters. This Imbert,¹ thinks is due to the rupture of the surrounding capsule, thus giving an exit for the further growth and invasion of the tumor cells.

According to Eliaseheff,² the first man who recognized a mammary cancer in the male breast, was Thom. Bartholinus (1616-1680). Then later J. Muratt and Gottfried Bidloe, both of whom lived in the 18th century, saw and described cancers of the male breasts. The literature of the present dates from Poirier's³ thesis (1883), and this together with Schuchardt's careful analyses in the "Archiv für Chirurgie"⁴ form the chief sources of our knowledge of this condition.

Up to 1890 Schuchardt had collected from every source and tabulated 472 cases of carcinoma of the male breast. He carefully reviewed all the literature and made elaborate statistical researches, particularly with regard to the relative frequency of occurrence in the sexes and the relation of deaths due to this disease per 1000 of population in the large cities of Europe. These statistics are so full that I shall not review them, as the original articles are readily obtained. Williams⁵ in 1889 reported 100 cases, but as he did not give the sources of his statistics, it is probable as Schuchardt remarks, that some cases were reported twice.

I have collected up to the present time the cases reported

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since 1890. I could find but 32 cases. To these I shall add 5 cases reported for the first time, 4 occurring in the Johns Hopkins Hospital, and 1 case I observed with Dr. T. P. Waring, of Savannah, Ga.

As to the relative frequency of this affection in the two sexes, statistics vary at times considerably. Thus, Schuchardt gives percentages from 1.6 to 8.4, obtained from various clinics. Bryant says cancer in the female is 100 times as frequent as in the male. Williams found it 117 times as frequent. In this hospital, between the years 1888 and 1901, there were admitted, on the surgical side, 307 cases of cancer of the breast, of which 3 were in males. 1 case was admitted to the medical wards. In St. Thomas' Hospital Reports (England) for the years 1891-1899 inclusive, there were 287 cases of cancer of the breast, 2 of which occurred in males.

Age.—In my series of cases the age of the patients was given in 36 cases. The majority, 25, occurred between the ages of 40 and 70. The youngest was 12 years (Blodgett⁹), the oldest 91 years (Lunn⁷). The greatest number occurring in any one decade was 13 in the 7th decade. This is somewhat later than most statistics give, the 5th and 6th decades seeming to be the time when cancer is most prone to occur.

Length of time the tumor was noticed.—The longest time was 35 years (Owens and Eisendrath⁸). The shortest time 2 weeks (Moore⁹). The former was the case of a merchant æt. 56, who was seen in 1898. Since 1863 he had noticed a slight depression of his right nipple, and a small swelling, the size of a pea, in the breast. This lump did not increase in size until 1897, when a small scab formed on the nipple, which, when removed, left a bleeding surface. No history of trauma. From that time the tumor steadily increased in size. In the other case there was a history of a blow 4 months before patient was seen. Six weeks after he was struck on the breast, a small painless lump appeared in the right breast. This gradually increased in size. At operation the whole breast was removed and the microscopical examination showed it to be a carcinoma.

Affected breast.—Either breast may be affected indifferently. Some statistics show that the left breast is more often the seat of tumor, others the right breast. Thus in Sengcnisse's paper he gives the following: Left breast, 17 out of 30 cases (Horteloup); 23 out of 37 cases (Poirier). In Williams' cases out of 71 there were 38 in which the right breast was affected, and Imbert¹⁰ gives 64 on the right side to 48 on the left. In my 37 cases, 18 occurred in the right breast and 18 in the left. In one case (Sinha¹¹) it was not stated which side was affected.

Trauma.—Out of the 37 cases, in 8 cases there was a definite history of injury to the breast at some time previous to the development of the tumor. No history in 4 and in 25 no statement was made as to trauma. Two cases were apparently caused by the irritation of constant friction. One, a shoemaker, æt. 91, who noticed that his braces rubbed his breast and made it tender (Lunn), and the other a patient, æt. 70, with a similar history (MacLaren¹²). One case (Imbert¹³) was thought to have developed cancer from the wearing of a

heavy watch over the right nipple. Schuchardt gives 25 out of 219 cases due to contusion or other mechanical cause.

Imbert¹⁴ says that he often found in those males who have cancer there is abnormal development of the breasts. In the case he reports the patients' breasts were much larger than normal. He thinks there is a relation between hypertrophied breasts and cancer. In none of the other cases was any mention made of enlargement of the breasts other than that due to the tumor itself.

Pain.—Pain was not a prominent symptom in the cases. It was noted only 9 times. In several it was of a lancinating character, and in one case described as gnawing. In 5 cases it was stated that there was no pain. I think we might assume that where pain was not a symptom nothing was said about it, and we can then take the remaining cases, 23 in number, making 28 cases in which there was no pain.

Ulceration.—Ulceration was given in 13 of my cases. In Schuchardt's series of 219 cases, in 70 it was stated whether or not ulceration occurred, ulceration being present in 61 cases. In nearly every case where the tumor had remained latent for a long time, some irritation caused its rapid enlargement with, at times, ulceration. Imbert says that ulceration is commonly preceded by the tumor's becoming adherent to the skin. This is thinned, becomes purple and enlarged veins are seen upon the surface. This is illustrated in all the cases reported that ulcerated. Those cases in which the skin over the tumor was described as being thin, purplish, etc., were undoubtedly seen soon before the ulceration of the tumor.

Retraction of nipple.—Retraction of the nipple was noted in 12 cases. In 18 cases the nipple was involved. In one case the nipple was totally destroyed (Case II), in another case only part was gone (Mussey¹⁵).

Discharge from nipple.—This was noted once. In 91 of Williams' cases there was discharge in 7. It was sanious in 4, puriform in 2 and lactiform in one. In the female, Gross¹⁶ gives 15 out of 207 cases. In 3 cases the nipple was noted as normal. In one of these cases (Powell¹⁷), although the tumor was quite near the nipple, the latter was not involved.

Enlarged axillary glands.—Out of 29 of the 37 cases the axillary glands in 20 were enlarged and palpable. In one case of 6 months standing, there were no glands felt. In one that had been noticed for 9 months there was one gland enlarged just at the anterior border of the axilla.

Macroscopical appearance.—There was nothing particularly interesting in the gross appearance of the tumor. The crater-like ulcer, with hard everted edges was described twice. The tumor was always described as hard, at times as "stony" hard. The size varied from a small lump that one could just feel, to a large, ulcerating swelling the size of an orange.

Microscopical appearance.—The microscopical appearances of the tumors in both sexes are quite similar. Thus far no peculiarities of structure in the male cancers have been made out. If we accept, for convenience, Billroth's classification of carcinomata of the breast¹⁸ into (1) acinous; (2) tubular; (3) atrophic or scirrhus; (4) gelatinous, we find that the majority of the male cancers are of the tubular type or, as he calls

them, carcinoma simplex. Mr. Marmaduke Sheild states that the usual type of cancer of the male breast is the hard spheroidal acinous variety. These would appear to be contradictory statements, but on close examination the difference is only in the nomenclature, which seems at present to be in a chaotic state. In Williams' statistics¹⁹ he found out of 100 cases 88 were of this type. 3 were classed as encephaloid; tubular, not in the sense in which Billroth classifies tumors, but the cylindrical-celled duct cancers, 6. He also found 3 squamous celled epitheliomata and one he calls melanotic. He states that the cylindrical-celled duct cancer is relatively more common in men than in women, while Lunn,²⁰ commenting on his case, remarks that this variety is very rare.

Of the 37 cases a microscopical examination was made in 26. Of these, 5 are called simply carcinomata. Of the remaining 21 cases, 2 were cylindrical-celled duct cancers, 11 were classed as scirrhus cancers, the descriptions in the main coinciding with that of Billroth's tubular variety or carcinoma simplex, 7 alveolar (Billroth's acinous type). Three of these were medullary cancers. Four of my cases examined under the microscope were carcinomata simplices, although the clinical history in one was very suggestive of a true scirrhus (Case III).

Operation.—34 cases were operated on. Of the 3 remaining, one (Murray²¹) was too extensive for removal and the other two, Case IV and one of Delacour's²² cases, refused operation. All of the patients operated on recovered from the immediate effects of operation, except in the case reported by Lunn of the old man who, a few days after removal of the tumor, died from "hypostatic congestion of the lungs." In Mussey's²³ case, 10 months after operation the patient was quite well. The boy, 12 years old, (Blodgett) was well 5 years after removal of the growth, which was a "typical carcinoma and had invaded all the visible gland tissue of the breast." Boelhagen,²⁴ who reported in his Dissertation 11 cases, followed up the course of events in 10. Three of these died. One died 3 years after operation, whether from a recurrence or not, was not known. The other two died of recurrence, one 1 year after operation, the other 5 years after. In both of these cases only a portion of the pectoralis major muscle was removed, although in the former there was a macroscopical growth in the substance of the muscle. The axilla was thoroughly dissected out and all glands removed in both cases. Of my 5 cases the results are known in 4. Two died; one 1½ years after removal (see Case III); the other 1 year and 5 months after operation (see Case I). The other two cases are at present well, but the operations were done comparatively recently (8 months and 3½ months ago), so nothing can be inferred from them.

A most interesting case and one showing a not infrequent sequela of cancer of the breast occurred in this hospital. This case I shall report in full, as there was a careful autopsy made, as well as microscopical sections of the original tumor and metastases.

Case I.—W. L. C. B. Surg. No. 8117, æt. 47, was admitted September 15, 1898, complaining of tumor of the left breast.

Family and past history have no bearing on the case. His trouble he dated back 26 years, when he was 19 years old. At that time he slipped on a fence and struck his breast. About a month later he noticed a lump about the size of a pea which gave him no pain or inconvenience, gradually increasing in size, until 3 years before admission the tumor took on a much more rapid growth and began to spread out. In the summer of 1897 he accidentally cut it with a suspender and noticed then that the growth was flattened out and about the size of a silver dollar. The tumor steadily grew larger and was sore when struck or handled roughly. In the winter of 1897 he noticed for the first time a lump in the axilla the size of end of thumb, which grew gradually to size of walnut without giving him any pain. He saw also that the nipple was being retracted and the skin over it was adherent. There was no discharge from the nipple, when the tumor was cut; only blood came from it. Patient had lost about 10 pounds and felt that he was becoming weak.

Physical examination showed him to be a fairly well nourished man. Occupying the nipple region and left areola was a disc-like stony hard growth measuring 2.5 x 3 cm., with a slightly scalloped, distinctly elevated, sharply defined margin. Radiating out from this in skin were fine purplish venules. The nipple was flattened out and retracted, and the growth projected about 2 cm. above skin level. The skin over most of the tumor was glistening and parchment like. The axilla was a contracting metastasis, and 3 or 4 small glands could be felt between it and the tumor. The pectoralis major muscle seemed drawn together and flattened out, although the tumor and metastases were movable on the deep structures.

Complete operation, including excision of the glands in the neck was done under ether Sept. 21. Axillary flap to cover axilla and skin graft to cover chest wall. The skin grafting took well and wound healed per primam, except for a small slough at lower angle of axillary flap. Patient was discharged well Oct. 2.

On Oct. 18 patient returned complaining of considerable pain in the epigastrium and around the xiphoid, shooting along costal margin to each side and coming on in paroxysms, at times so severe that he was kept awake the greater part of the night. His pain had no relation to the taking of food, he had no nausea or vomiting, nor was there any marked loss of appetite or strength. He complained of no pain in the wound. The area where the slough was, was covered over in great part by healthy granulations. He remained in the hospital until Oct. 23, when he was discharged improved, although there was still some pain along the costal borders.

He returned again Nov. 3 complaining of similar pains and stiff back. He remembered that a month before operation he had had some pain in his lower right axilla, passing to ensiform cartilage. Now, however, he was suffering from girdle pains of a shooting but sometimes burning or aching character, along the course of the 9th and 10th ribs. The rigidity of his back was noticed for 2 weeks and was gradually growing worse, so that he could not stand on his feet for long

nor could he stoop. On examination there was marked rigidity of the spinal muscles, but no curvature or deviation of the spine. At his own request he was discharged Nov. 5.

Again patient returned Feb. 6, 1899, complaining of the girdle pains and trouble with his bladder. The attacks of pain would come on in acute paroxysms, forcing patient to double up with knees on chest.

Now began the onset of his paraplegia, with stiffness in the left knee and a feeling in the soles of his feet as if he were walking on cotton.

On examination there was seen prominence of the 6th to 9th dorsal vertebrae with a small, red fluctuating, very painful mass about the size of an almond at the level of the 8th spine.

Patient now became gradually worse. He had dribbling of urine from an overdistended bladder and was troubled with priapism. It was necessary constantly to catheterize him. There was almost complete paresis of his legs which became complete shortly before death. There was also some dulling of sensation to pain and touch over lower legs anteriorly. His pain was so intense that chloroform was constantly administered. The prominence of the dorsal spines became more marked and there was also distinct enlargement of the spines.

Patient gradually sank. He became delirious and coprolalic. At no time were his arms affected. The deep reflexes in his legs which had at the onset been present with later development of ankle clonus, were completely lost. Bedsores developed over sacrum and heels and he died February 27, 1899. At autopsy there were no metastases to the internal organs, but portions of the sternum, ribs and vertebrae were the seats of metastatic deposits. These growths filled the interior of the bone, leaving only a surrounding thin shell of bone, and on section were composed of dark purplish masses in which spicules of bone were seen. The consistency was semifluid. The spinal cord was removed and revealed on the anterior floor of the canal a mass directly over the 7th dorsal centrum. This mass was somewhat saddle-shaped, measuring 2 cm. long and 1.5 cm. broad, extending almost across the canal, projecting into it and causing a well marked compression of the cord. There were several other small nodules above and below this projecting into the canal, but they probably exerted no pressure on the cord.

At the point where the tumor encroached on the cord there was a definite compression with softening and narrowing antero-posteriorly to about one-half thickness of adjoining portion.

Microscopical sections were made from the original tumor, from a nodule in one of the ribs, from the mass along the spine, axillary and bronchial glands and from the mass projecting into the spinal canal. Section of the breast shows a tumor composed to large extent of connective-tissue stroma with the tumor cells scattered in groups here and there. Some areas show spaces lined by one or more rows of epithelial cells which appear as cross sections of tubes having definite lumina. In other areas are strands of cells, while in other parts dense masses of cells are seen which have in

many places shrunk away from the surrounding connective-tissue wall. In some parts of the sections are seen large masses of cells having the typical vesicular nuclei and relatively large amount of protoplasm with very little connective-tissue stroma. Everywhere, especially at periphery of tumor, is seen round-cell infiltration. Sections through the pectoral fascia and muscle show the former is infiltrated with the tumor cells but the latter contains none.

Several axillary glands were studied and metastases were found in some. Sections from a bronchial gland show cells similar to those of the primary tumor arranged in acinous forms. There is very little connective-tissue stroma. At the periphery of the nodule the tumor cells can be seen infiltrating the gland substance.

Sections of the marrow of a rib and a diseased vertebrae and from the mass along the spines show dense infiltration with the tumor cells.

A section from the growth in canal is seen to be composed entirely of cells similar to, but smaller than, the original tumor cells, and connective tissue strands separating these cells into alveolar-like spaces. Microscopical diagnosis, carcinoma simplex.

CASE II.—D. M., Surg. No. 10,721, æt. 71, admitted July 29, 1900, complaining of swelling of breast. Family and past history negative. 16 months before admission he noticed a lump on the right nipple which grew to the size of a strawberry, which was removed with cancer paste and he thought himself cured; 2 months later the growth returned and progressively increased in size. He suffered with stinging pain which kept him awake at night. Since his illness he had lost 40 pounds in weight.

Physical examination showed patient to be a large, corpulent man. Occupying region of right breast was a tumor projecting 4 cm. above the chest wall, oval in shape 5 x 7 cm., with ulcerated surface and having a foul odor. The tumor completely surrounded the nipple area and the nipple itself had disappeared. Skin around it was tense and red, tumor was not very hard or tender and was not adherent to underlying structure. Enlarged glands in axilla. Operation was performed consisting of complete removal of the breast together with both pectoral muscles and a thorough dissection and removal of the glands in the axilla and lower part of neck. Patient made an uneventful recovery and is at present well.

Sections from this tumor showed pictures quite similar to those from Case I except that the tumor was more cellular. Numerous mitotic figures were seen. One could surely say from these sections that this tumor was of an exceedingly malignant character. A section from the subjacent muscle shows metastasis. Scattered throughout the tumor were areas of hyaline degeneration of the cells. Several glands were examined but no metastases were seen. Diagnosis: Carcinoma simplex.

CASE III.—P. S., Surg. No. 2628, æt. 64, admitted November 14, 1893, complaining of swelling in left breast. 20 years before he sustained an injury to the breast which made it

always painful and tender. 5 years later he noticed a lump near the nipple. During two weeks before admission the swelling had increased rapidly and was tender on palpation. The nipple was retracted and the skin over the tumor was adherent to it and was dimpled and reddened. Nodule was also adherent to fascia beneath. Tumor was situated in inner and upper quadrant, measured 1.5 x 2.5 x 1.75 cm. Axillary glands palpable.

Operation November 16. Breast with pectoralis major muscle and axilla removed "en masse." Patient did well and was discharged cured. He returned November 8, 1894, with nodules over site of old scar and a few palpable glands over right clavicle. These were removed under cocaine and patient discharged well. Patient did well until spring of 1895. Then he gradually became weak and lost flesh and strength. No pain or discomfort. He had no sensation of hunger and ate very little. There was no dyspnea, no pleural pain. He became weaker and weaker and swallowing was almost impossible. A distinct nodule was felt at this time in abdomen below costal margin. He died in May, 1895, 1 year and 6 months after operation. Autopsy showed carcinomatous nodules in all the internal organs and in the lymph glands. At the cardiac end of the stomach were a number of nodules. Along the lesser curvature these had produced a stricture at the cardiac orifice. No metastases to the peritoneum.

Sections from the tumor, glands and nodules removed from the skin showed picture resembling that of Cases I and II. The tumor cells were arranged in larger areas and there was very little stroma substance in one section of a lymph gland. Diagnosis: Carcinoma simplex.

CASE IV.—Full notes of this case were lost. I am indebted to Dr. Osler for the following facts. E. S., æt. 40, was admitted to Ward C with a history of severe girdle pains and pains in the legs for several months. When seen he was rapidly becoming paraplegic, had a great deal of pain and had lost much weight. In the right breast he had a well marked scirrhous tumor, which had not previously been recognized, and which had given him no trouble. He refused operation.

CASE V.—I saw this case with Dr. Waring December 22, 1900. M. G., school teacher, æt. 50. For a number of years he had been suffering with a form of nervous dyspepsia. Patient said he did not know how many years he had had a lump in the left breast. He thought he had injured the breast before he noticed the tumor. It had begun to grow rapidly in last few weeks. He had occasional sharp pains in the breast and the tumor was very tender on manipulation. The tumor was situated in upper and outer quadrant. The nipple was retracted. The tumor was about the size of a walnut and was firm, hard, and slightly nodular. It was adherent to the skin but could be freely moved over the deeper structures. No axillary glands palpable.

Operation consisted in removal of tumor and subjacent pectoral fascia by an elliptical incision. The pectoral fascia was infiltrated for some distance from tumor. Wound sutured. Healing per primam. Patient is at present well.

Microscopical sections were made and examined. The pictures corresponded to those seen in sections from Case I, so that description will serve here. The pectoral fascia in this case was infiltrated with the new growth.

Finally, there is practically no difference between the condition in the two sexes. The clinical symptoms are quite similar, the pathological findings are alike and thus far the microscopical examinations of the tumors removed from men and women have shown no difference in structure.

All the varieties found in women are found in men, but it appears that the atrophic scirrhous carcinoma is much more common in women. The figures also show that in men the nipple is more apt to be involved, possibly because the gland is so small that any growth must of necessity be near enough to the nipple eventually to cause its retraction. Ulceration would appear to be more common in men, while discharge from the nipple is relatively more frequently seen in women (Gross, 15 out of 207 cases). Pain, while at all times a variable symptom, is not so great in male as in female cancer (Imbert), although it can be of an excruciating character as seen in several cases reported in the literature.

It is interesting to note that in my first case, although there were many metastases in the bones, none of the organs were affected, whereas in another of my cases (Case III) autopsy showed carcinomatous deposits in all the organs with a nodule at the cardiac end of the stomach, causing stenosis of the orifice. The bones in this case unfortunately could not be examined but it is probable from the history that they were free from metastases. In still another of my cases (Case IV) the patient came to hospital complaining of girdle pains in the legs which for several months had been severe. He was rapidly becoming paraplegic and had lost much weight. He did not know he had a tumor of the breast, which was found on making the physical examination. It is within reason to suppose that he had a condition similar to my Case I, with metastases in bone but none in the internal organs.

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REPORT OF A CASE OF CARCINOMA DIAGNOSED BY MEANS OF PARACENTESIS ABDOMINIS, WITH SOME REMARKS ON THE DIAGNOSTIC VALUE OF EXAMINATIONS OF SEROUS EFFUSIONS.

BY WALTER RALPH STEINER, A. M., M. D., Hartford, Conn.

Formerly House Medical Officer of the Johns Hopkins Hospital.

The following case is reported because of the accidental method of diagnosis.

Fannie C., negro, aged 63 years (Hospital No. 25,015), was admitted to the Johns Hopkins Hospital, December 15, 1899, complaining of pain and swelling of the stomach.

Family history.—Negative.

Past history.—Measles and chicken-pox as a child. Small-pox thirty-seven years ago, having contracted it during an epidemic of this disease in Baltimore. About thirty years prior to admission to hospital she had some ill-defined womb trouble, for which she received treatment. Denied syphilis. Was generally a moderate beer and whiskey drinker, but at times had drunk to excess.

Present illness.—During July and August, 1898, she noticed her "stomach" would swell after eating but would go down again in an hour or two. This continued daily until about eight weeks ago when she observed the swelling did not decrease in size but kept constantly growing larger. About this time, also, she began to complain of sharp pains in the pit of her stomach. They would frequently radiate to the back and obliged her to stop work. Since then she had suffered a good deal from coughing and shortness of breath. Both were aggravated by exertion, so she had spent most of her time in bed or sitting up in an easy chair.

For six weeks past she had had a burning dull pain, from umbilicus down to pelvis, just before micturition. Apparently there was no increase in frequency or in the amount of urine voided. She was, as a rule, constipated and frequently had to take remedies for it.

For two weeks she had noted a slight white, non-irritating,

vaginal discharge—the first since her menopause, eighteen years ago.

Physical examination.—The patient was a well developed, well nourished mulatto woman. There was no cyanosis, no respiratory distress and no cough during examination. The lips and mucous membranes were of good color. The tongue was tremulous and coated with a thin white fur.

Thorax somewhat barrel shaped. Respiratory movements fair and equal. Costal angle normal.

On palpation the vocal fremitus was diminished in the lower right axilla and over the lower left lobe in the back. It was absent over the lower right lobe behind. On percussion the note was impaired where the vocal fremitus was diminished and there was slight movable dullness in the right front. Over the lower right back the note was quite dull. On auscultation the breath sounds were enfeebled where the note was impaired and fine and coarse moist râles were here heard. The breath sounds were absent on the lower right back and the vocal resonance here had a nasal quality.

Heart not enlarged. A soft systolic murmur was heard at the apex, which was not transmitted upwards or outwards. The pulmonic second was somewhat accentuated. Pulse 94 to the minute, regular in force and rhythm, and of good volume and tension. Arteries not thickened.

Abdomen very much and symmetrically distended. The veins in the lower quadrants were quite prominent and swollen. The costal and iliac grooves were absent. There was marked bulging of the flank lines and also of the dependent parts on changing position. On palpation fluctuation was easily obtainable. On percussion there was dullness in the

dependent parts, with movable dulness when she changed her position.

Extremities.—Feet and legs were very œdematous and pitted easily on pressure.

On December 18 a vaginal examination was made by Dr. Hunner with negative results. The note does not state whether the ovaries were palpated.

The day following, patient's abdomen was tapped, the trochar being inserted in the median line, midway between umbilicus and symphysis pubis. 8000 cc. of a dull red fluid were withdrawn (see Chart I. for this and subsequent tapings). After the tapping Dr. Fitcher made the following note: "For the past two nights patient has had some rise of temperature. On December 18, her temperature was 102° at 8 p. m., and on December 19, at the same hour, it had risen to 103.2°. She has had no distinct chill.

"The abdomen is still markedly distended. The costal and iliac grooves are symmetrical. There is marked bulging in the flanks. On percussion the note is tympanitic in the elevated but flat in the dependent portions. There is still considerable fluid in the abdomen and distinct movable dulness is obtainable. The relative hepatic dulness begins over the middle of the sixth interspace, and the absolute over the middle of the seventh interspace, and extends to a point 8.5 cm. below the costal margin in the mammary line. The total extent of absolute dulness measures 14 cm. On palpation a definite mass is felt, occupying the lower part of the epigastric and the upper part of the umbilical regions. The fingers can be distinctly placed below the margin of this mass, which extends over to the right and becomes continuous with a resistant mass in the lumbar region of the abdomen. From this mass it is separated by a more or less distinct notch, somewhat resembling the notch in the liver. The fingers can be pressed in above the mass in the epigastrium. To the left the outline of the mass is less distinctly made out, but it appears to terminate at the junction of the upper quadrant of the umbilical with the lumbar region. The surface of this mass, as well as its lower border, is very nodular and rather hard. To the right its margin is not definitely to be made out. The lower margin of the tumor descends slightly on deep inspiration but does not feel as if connected with the liver. The mass is very freely movable in both vertical and transverse directions. It seems to be separated from the abdominal wall by a thin layer of fluid. After inflation of the stomach, the mass becomes more prominent and descends distinctly. Its lower margin is now well felt 4 cm. below the umbilicus in the median line. The tumor is extremely nodular; this is more marked than before distension. The upper limit of stomach tympany begins at the sixth interspace on the parasternal line. The lower limit of stomach tympany reaches 4 cm. below the umbilicus in the median line, at the lower margin of the tumor. Over the tumor area dull tympany is obtained on percussion. There is no definite peristaltic wave to be made out. No definite glands palpable in the supraclavicular fossæ or in the episternal notch. The axillary glands are not enlarged, nor are the inguinals espec-

ally increased in size." The rectal examination was practically negative.

On the next day Dr. McCrae described the tumor as an almost continuous succession of nodular masses which were best felt on deeper dipping. He made out the total extent of these masses to be 21 cm., reaching from the right mammary to the left parasternal line. No tumor was felt in the costal angle or emerging from the left costal margin. Dr. Osler described these distinct nodular masses as separate from the stomach, which was palpable on inflation.

January 10. Patient's stools were examined for tubercle bacilli with negative results. They had been very watery and chocolate in color for some days previous. No excess of fat was made out by microscopic examination.

Three days later a blood examination gave the following: red blood corpuscles 5,608,000; white blood corpuscles 4400; hæmoglobin 68 per cent.

A few days before January 31 she had complained of pain in the right side and shortness of breath. On that day the percussion note was flat over the right lung almost from apex to base, in front and behind. The vocal fremitus was slightly exaggerated below the right clavicle, but elsewhere it was diminished. The breath sounds over the upper right front had a slightly tubular, amphoric quality, and the voice sounds throughout were somewhat diminished and of a distinct nasal quality. There was appreciable movable dulness over the first interspace. The point of maximum cardiac impulse was in the sixth interspace 11.5 cm. from the mid-sternal line. The heart's action was rather rapid, and the rhythm was suggestive of embryocardia. Later in the day the right pleura was aspirated, the needle being inserted a little to the left of the angle of the scapula, in the eighth interspace. 1550 cc. of a thin hæmorrhagic fluid were withdrawn (see Chart II. for this and subsequent aspirations). The point of maximum cardiac impulse as well as where the sounds were best heard could not be well determined after this aspiration. They seemed to be well within the measured spot given above.

Feb. 18. *Blood examination.*—Red blood corpuscles 4,522,000; white blood corpuscles 14,000; hæmoglobin 58 per cent. Five days later she complained of passing a considerable quantity of blood in her stools. From this time on her condition gradually grew worse. On March 13 an emphysematous condition of the abdominal wall was noted, and the œdema here and in the extremities was most marked. Two weeks afterwards she began to have severe attacks of vomiting and could retain nothing on her stomach. This was relieved by tapping. Micturition now became somewhat difficult and she was only able to void very small quantities of urine at one time.

April 7. *Blood examination.*—Red blood corpuscles 4,476,000; white blood corpuscles 10,000; hæmoglobin 60 per cent. Differential count:

Polymorphonuclears	82.
Large mononuclears and Transitionals....	7.5
Small mononuclears	10.
Eosinophiles5

About this time she began to expectorate very profusely. The sputum was clear, watery and frothy in character, with a slight whitish sediment. No tubercle bacilli were found on examination.

On April 10, on putting the trochar through the canula, after a tapping, a small piece of tissue, 5 x 1 mm., was noticed at the end of the trochar. It was white in color and looked very much like fibrin. Thinking, however, it might be of some diagnostic import, we hardened it in alcohol and finally imbedded it in celloidin. The sections were stained with hæmatoxylin and eosin. Their examination will be later mentioned.

The patient grew gradually weaker and became somewhat emaciated. During her last month she was obliged to remain in bed. Dr. Futeher made the following note on May 22: "Patient's temperature has been gradually falling during the past four days. This a. m. at eight it is 96. Pulse is irregular and extremely weak, almost imperceptible, 25 to the quarter. Owing to fulness and distension of the abdomen it is practically impossible to make out the mass, which has been felt, except in the epigastrium a sense of resistance is encountered. The œdema of the abdominal walls is considerable. There is flatness over the right lung as high as the third interspace, above which the voice sounds are harsh and

exaggerated. The respiratory murmur below is feeble, distant, and of a suggestive tubular quality. The apex beat is in the fifth interspace, 2 cm. inside the mammary line. The heart sounds are well heard at apex and base. There are no endocardial murmurs. The second pulmonic is accented."

The week before her death she failed very rapidly. She died on May 27 at 7.15 a. m.

Urine.—On entrance the urine was dark amber in color, cloudy, 1025 in specific gravity, acid on reaction, negative for sugar and albumen. There was a heavy, grayish, flocculent precipitate. Microscopically a few hyaline and granular casts, as well as many epithelial cells, red blood corpuscles, white blood corpuscles, and mucous cylindroids. The bile test was negative. The subsequent examinations did not vary much from the above save that albumen was generally found as a trace.

Temperature.—This varied between 100° and normal till December 18, when it rose to 102° (see Dr. Futeher's first note. It fell to normal December 20 and ranged about as before till January 7, when it rose to 101°. Then it varied generally as before, but occasionally was subnormal till April 8. It rose on this day to 101.4°, but fell in two days and remained as before until May 18. From this date on it was subnormal.

CHART I.—EXAMINATIONS OF THE ASCITIC FLUID.

	I. Dec. 9.	II. Jan. 7.	III. Jan. 19.	IV. Feb. 7.	V. Feb. 27.	VI. March 11.	VII. March 20.	VIII. March 27.	IX. April 3.	X. April 10.	XI. April 18.	XII. April 25.	XIII. May 5.	XIV. May 14.
Amount . .	8000 cc.	6500 cc.	4000 + cc.	6800 cc.	6420 cc.	7000 cc.	7020 cc.	4800 cc.	10,000 cc.	8000 cc.	7020 cc.	7000 cc.	6400 cc.	5000 cc.
Color and character- istics . . .	Dull red.	Reddish yellow, cloudy.	Yellowish red, cloudy.	Reddish yellow, cloudy.	Reddish green, cloudy.	Amber, cloudy.	Orange yellow, cloudy.	Lemon yellow, cloudy.	Reddish yellow, cloudy.	Reddish yellow, cloudy.	Reddish yellow, cloudy.	Reddish yellow, cloudy.	Reddish yellow, cloudy.	Reddish yellow, cloudy.
Reaction	Neutral.	Slightly alkaline.	Neutral.	Alkaline.	Alkaline.	Alkaline.	Alkaline.	Neutral.	Neutral.
Specific gravity	1018	1019	1020	1017	1015	1014	1015	1014	1019
Sediment	Flocculent.	Reddish black.	Slight white.	Red, with fibrin flakes.	Red, with fibrin flakes.	Red, with fibrin flakes.	Red, with fibrin flakes.	Red, with fibrin flakes.	Red.
Albumen	2.25%	2.8%	2.5%	2.5%	3.5%	Present, a'mt not stated.	3%	1.7%	Present, am't not stated.
Sugar	None.	None.	None.	None.	None.	None.	None.	None.	None.
Microscopically	Numerous red blood corpuscles; some leucocytes. No epithelial cells.	Numerous cells, varying in size from 1 to 4 diameters of a red blood corpuscle, mononuclear in type and containing many fat globules. The cells occur singly or in clumps.	Numerous mononuclear cells as in the second examination. Many red blood corpuscles.	Some red blood corpuscles; few leucocytes.	Many red blood corpuscles; few leucocytes.	Many red blood corpuscles; some leucocytes; fibrin.	Many red blood corpuscles; few leucocytes.	Many red blood corpuscles; few leucocytes.	Many red blood corpuscles; few leucocytes.	Many red blood corpuscles; few leucocytes.

CHART II.—EXAMINATIONS OF THE PLEURAL EFFUSIONS.

	I. January 31.	II. February 23.	III. April 12.
Amount	1550 cc.	1200 cc.	600 cc.
Color and characteristics.....	Yellow, cloudy with flakes of fibrin, colored red.	Blood red, cloudy.	Blood red, cloudy.
Reaction.....	Alkaline.	Alkaline.	Alkaline.
Specific gravity.....	1017	1010
Sediment	None visible.	Thick red.	None visible.
Albumen	3.5%	4.5%	1.5%
Sugar	None.	None.	None.
Microscopically	Many red blood corpuscles.	Many red blood corpuscles.	Many red blood corpuscles.

Abstract of protocol. *Anatomical diagnosis.*—Carcinoma of ovary. Secondary implantations on peritoneum. Involvement of right pleura. Ascites and hydropericardium. Compression of lung. Secondary nodules in liver, intestine, etc. Obliteration of appendix by tumor mass. Myomata uteri.

Autopsy by Dr. MacCallum. Body of a large woman, 163 cm. in length. Great œdema of legs and abdominal walls; well marked œdema of left hand.

Peritoneal cavity contains large quantities of smoky, turbid fluid. Peritoneal layers are much thickened. Parietal peritoneum is roughened by a rather congested, semi-translucent, new growth. There are small depressed areas here and there resembling ulcers, the bases of which are smooth and clear; the tissues dividing these ulcer-like places are shining and scar-like in character.

Omentum drawn up into a firm mass over the level of the transverse colon and forms a transverse group of hard nodules which have a rather translucent appearance, and are studded with opaque, yellowish masses. Intestinal coils not especially adherent but serous surfaces, as well as serous surfaces of mesentery, are everywhere studded with nodular masses, varying in size from pin point to size of a bean; these have spots of opacity. There are a few adhesions between the coils of intestine lying over the fundus of the uterus and the bladder. The appendix is obscured in a firm mass of the tumors. The under surface of the liver is bound by adhesions to the stomach and transverse colon. There is great thickening of the peritoneum over the under surface of the liver. The upper surface of the liver is densely adherent to the diaphragm.

Right *pleural cavity* contains a large quantity of blood-stained fluid.

Pericardium contains a small amount of clear fluid. The pericardial layers are smooth.

Lungs.—The left pleural cavity contains a small amount of fluid. The pleural surfaces are generally smooth. Over pleura of upper lobe and upper portions of lower lobe there can be felt and seen pearly white nodules of pin-head size. The anterior portion of the left lung is air-containing.

There are two nodules in the anterior edge which have a firm consistence but show no changes in color; similar nodules at base of lower lobe. On section there can be felt throughout the lung numerous, minute, firm nodules which are somewhat pigmented. These masses are œdematous and apparently contain some alveolar exudate. Surface of the lung has a rather salmon pink color and is quite moist. Bronchi are somewhat congested; blood-vessels clear.

The right lung is very much compressed by pleural exudate and occupies an area limited below to the level of the third rib. The pleural layers exhibit the same nodular appearance described in peritoneal cavity. The lung is so much compressed that the lobes are indistinguishable; the lung substance on section is, in general, air-containing and rather leathery in consistence. The lower portion is soft and has a grayish, opaque appearance. The bronchi and vessels are much thickened and are very prominent over the whole cut surface. There are no tumor nodules in the lung. The costal pleura is very much thickened by the presence of tumor nodules and has rather a hæmorrhagic appearance with a ragged surface.

Spleen is bound down to diaphragm by old adhesions which have the same translucent appearance as the nodules already described. Weight 150 grms., measures 11 x 7 cm. Capsule thickened and opaque. On section the Malpighian bodies and the trabeculæ are well seen. At hilus is a rather whitish nodule, soft, and somewhat translucent, apparently part of the tumor. Similar pin-head sized nodules occur adjacent to the vessels in the pulp of the spleen. The spleen pulp has a rather brownish red color. On stripping away diaphragm from liver the former is found to be studded with tumor nodules which often correspond with nodules on the surface of the liver.

Vagina normal.

On attempting to dissect apart the pelvic viscera neither *ovary* can be correctly outlined. The *Fallopian tubes* are distended and congested and are partly imbedded in a mass of tumor substance.

Uterus is involved from without by the tumor nodules. Its wall also contains several small myomata.

Liver.—Weight 1400 grms. Measures 24 x 19 x 9 cm. The upper surface is much roughened by the growth of tumor nodules between it and the diaphragm. There are also numerous superficial nodules. Similar nodules, reaching a diameter of 2 cm., may also be found in the substance of the liver; they are rounded, white and semi-translucent. The liver, in general, shows evidences of chronic congestion. There are some translucent nodules about pin-head size.

Kidneys.—These showed nothing, save that over the surface of the right kidney a few opaque, rather yellowish nodules were seen.

Adrenals.—The left adrenal contains several yellowish nodules which lie in the cortex.

Stomach.—There are tumor nodules in the outer wall of the stomach but the mucosa is everywhere smooth.

Pancreas.—There are small nodules throughout the surface of the pancreas, otherwise it is apparently normal.

Great omentum.—The rolled up omentum forms a mass 21 cm. long and 6 cm. in diameter; this forms the largest and firmest of the tumor nodules.

Mesenteric glands.—The mesenteric glands in general are not much enlarged but apparently contain tumor nodules.

Intestines.—The mucosa of the whole intestinal tract is apparently normal except for a few sub-mucous nodules in the ileum; one of which seems to involve the mucosa. There are also a few ulcerated patches in the colon, probably due to changes produced by the invasion of the tumor nodules. The serous surfaces are everywhere thickly studded with nodules. In the position of the appendix there is an elongated tumor mass, at the base of which there is a cavity apparently lined with mucosa. This cavity cannot be further traced into the tumor mass.

Bacteriological examination.—The cultures from the peritoneal and pleural cavities were contaminated, but from the heart's blood the streptococcus pyogenes was obtained. The examination was otherwise negative.

Histological examination.—The tumor is an adeno-carcinoma with an irregular glandular structure, the epithelial cells being arranged in several layers. Some nodules in the liver are gland-like masses, very small and lined by one row of cells; others show masses formed by cells making alveoli in the stroma. The liver also shows extreme fatty degeneration. The lung shows well defined broncho-pneumonia and anthracosis. The kidney sections show moderate diffuse connective-tissue growth and parenchymatous degeneration of the epithelium. The sections from the intestines show a sub-peritoneal tumor, as well as a nodule imbedded in the muscular coat. In the subserous tissue well defined lymphatic spaces occur, filled with tumor cells. The spleen shows evidence of chronic interstitial splenitis and contains a well defined tumor nodule.

In considering the diagnosis of this case two diseases were chiefly thought of, viz.: tuberculous peritonitis and carcinoma. If the latter was the correct diagnosis it was impossible to conjecture the primary seat of the disease, as there were no symptoms on the part of any of the abdominal organs. The stomach or the ovaries seemed to be the most likely origin.

Numerous attempts were made to obtain a test breakfast, but the patient strenuously objected to the passage of a stomach tube, so this aid to diagnosis was consequently unavailing. It is to be regretted that the tuberculin test and animal inoculations with the serous fluid were not resorted to. The age of the patient and the presence of a vaginal discharge were in favor of the malignant nature of the disease. The vaginal examination was negative. There was no emaciation until about one month before death. All doubt as to the diagnosis, however, was dispelled when the piece of tissue, removed during a tapping, was examined microscopically.

During the past century the doctrine was stoutly maintained that cancer cells were characteristic: many claimed

to be able to diagnose a malignant tumor by examining the cells in a serous effusion. This theory, nevertheless, gradually lost ground, till now but few believe in it.

Dock¹ has made a valuable contribution to this subject and has shown that similar cells are found in cancerous, tuberculous, and other effusions. He, Rieder,² and Warthin,³ however, claim that the diagnosis of a malignant growth may be made by the presence of many cells in serous effusions showing mitoses. These mitoses may be typical or atypical in type. The distinction is a quantitative and not a qualitative one.

In our case, though centrifugalized specimens were frequently examined and a number of stained specimens of the dried sediment made, yet in no instance were such cells seen. On two occasions (see Chart I.) large mononuclear cells were observed, but through Dock's studies, we know they can be found in ordinary serous effusions. They were probably endothelial in origin.

In fixing the sediment on the slides, besides the usual means employed, Bahrenberg⁴ has used the following method: "After decanting the supernatant fluid, the addition of alcohol was followed by the changing of the more or lessropy sediment into a firm mass resembling coagulum. After a few days this material was firm and hard, and, after imbedding it in celloidin, thin sections were readily cut."

The specific gravity is an aid to diagnosis. In cancerous it is low, but in tuberculous effusions it varies between 1022-1026 (Dock). Exceptions, however, can be found to this statement for Bögehold⁵ and Quincke⁶ have reported cases where the specific gravity of the cancerous effusion was over 1022. In the former instance the presence of a large amount of blood might account for the high specific gravity. In our case the specific gravity of the ascetic fluid varied between 1014-1020, while that of the pleural effusion was 1010 and 1017 (see Charts I. and II.).

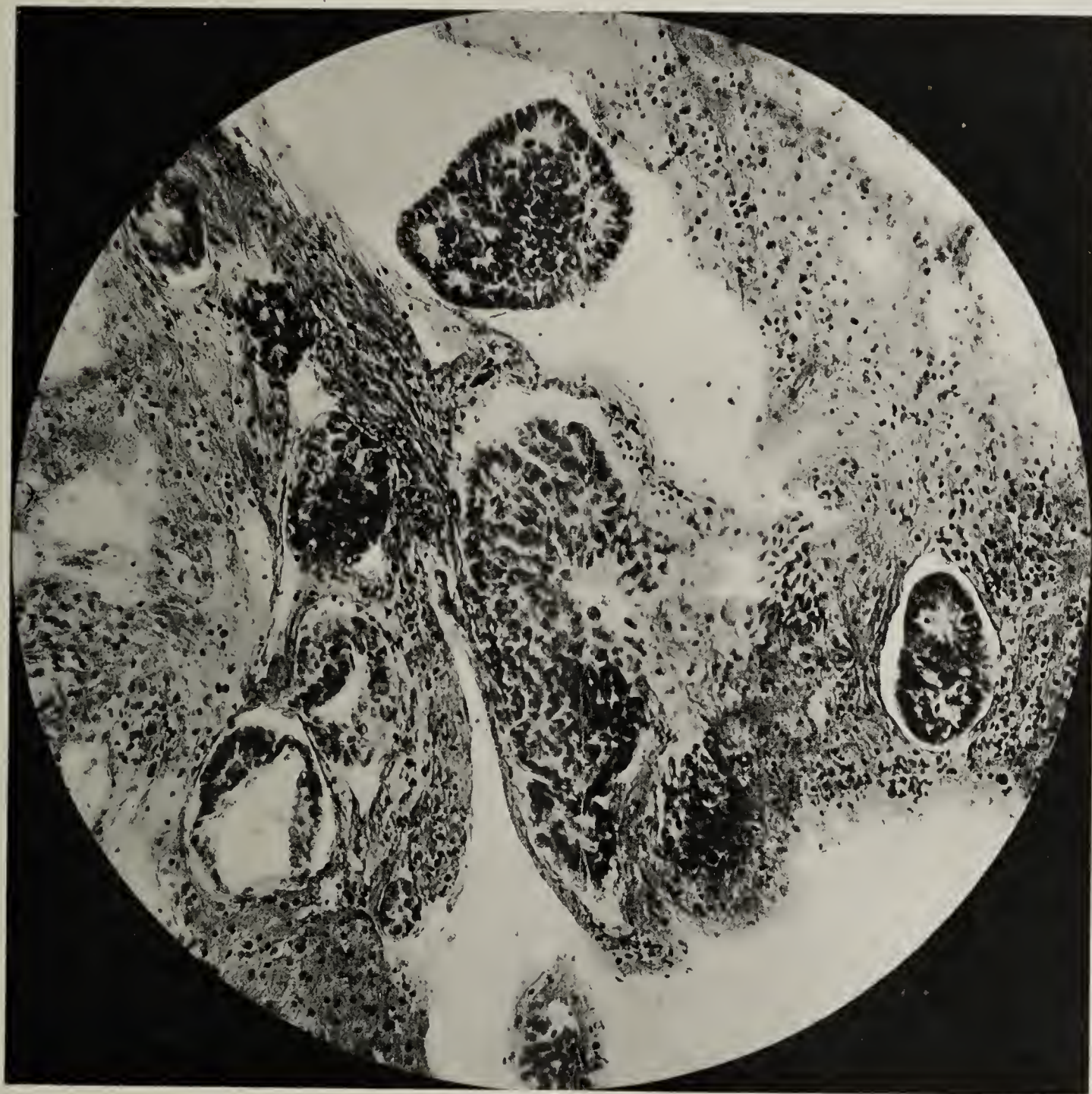
The accompanying illustration shows the microscopical appearance of the piece of tissue removed on April 10. The photomicrograph was taken by means of the Zeiss apochromatic lenses. The microscopical findings were as follows: Distinct alveoli are seen with lumina, more or less completely filled with polymorphous cells, containing large, round or oval, vesicular nuclei. The alveoli are glandular in type and their peripheries are lined by single layers of low cuboidal cells. The stroma consists of a loose meshwork of connective tissue fibrillæ infiltrated with lymphocytes. No plasma cells are seen. The diagnosis of adeno-carcinoma was made, which was subsequently corroborated at autopsy.

I have only been able to find four similar cases on record.

(1) Rieder⁷ speaks of obtaining a small piece of tissue from the puncture opening in the abdominal wall. The case was diagnosed sarcoma carcinomatosum.

(2) Lenhartz found in an ascitic fluid a pale transparent colloid nodule which showed the alveolar structure of a colloid carcinoma of the peritoneum.

(3) Prentiss has published a case in which the right pleural cavity was aspirated, but no fluid was found. "Instead only



× 570. Objective 6 mm. Compensat. proj. Ocular No. 6. Stain haematoxylin-eosin.

blood and a quantity of substance looking like partially organized fibrin was drawn out, evidently from the lung substance." This material was found on microscopic examination to be composed of masses of sarcoma cells. The autopsy confirmed the diagnosis.

(4) Girvin and Steele have recently reported a case of "carcinoma of the pleura, diagnosed by tissue removed in tapping."

In conclusion, I desire to thank Dr. Osler for allowing me to report this case, and Dr. Arthur J. Wolfe, of Hartford, for the photomicrograph which accompanies this article.

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A CASE OF PRIMARY ADENO-CARCINOMA OF THE FALLOPIAN TUBE.

BY ELIZABETH HURDON, M. D.

Clinical Assistant in Gynecology, The Johns Hopkins Hospital Dispensary.

New growths of the Fallopian tube were seldom mentioned by the older writers, and by some, primary tumors were believed not to exist. The descriptions of the early cases are so meagre that in most instances there is not sufficient evidence that the growth was not due to a metastasis from a tumor arising elsewhere. The first undoubted case of primary cancer was described by Orthmann¹ in 1888, and since then thirty-four additional cases have been recorded.

The tumor in most instances originates in the epithelium covering the folds of the mucosa and has, therefore, a well marked papillary structure. Friedenheim,² however, has described a case in which the tubal folds are practically normal, while the muscular coats are infiltrated with carcinomatous masses. This growth, as the writer suggests, probably originated in the gland-like structures, sometimes found in the tube walls.

Most observers are of the opinion that a close relationship exists between the development of the carcinoma and the presence of a chronic inflammatory process. It seems probable that this is an important predisposing factor, in many cases the characteristic changes resulting from an old inflammation were demonstrable and in some the opposite tube was converted into a sac containing serous or purulent fluid. The history of sterility so generally obtained and often definite attacks of pelvic inflammation tend to support this view.

Alban Doran³ believes that carcinoma is sometimes due to malignant changes in a simple papilloma, which itself may be traced to inflammatory disease. The case reported by

Kaltenbach⁴ and the first case of Fabricius⁵ possibly belong to this group.

Only a brief history of the present case could be obtained, and is as follows:

CASE No. 576, aged 63. Admitted to Dr. Kelly's private sanatorium March, 1898. Complaint, sanious vaginal discharge, elevation of temperature.

The patient had had four normal labors and had enjoyed perfect health until the summer before admission, when she suffered from an attack of typhoid fever, after which she noticed an almost constant blood-tinged vaginal discharge, and was subject to frequent rises of temperature. Examination under an anesthetic revealed an irregular mass about the size of a mandarin on the left side of the uterus. The tumor was of rather soft consistency and was adherent. The right tube and ovary were apparently normal. The uterus was small and on curetting no tissue was removed. Pyosalpinx was diagnosed and operation advised.

Operation.—Abdominal hysterectomy, right salpingectomy, left salpingo-oophorectomy. The right ovary, which was small and perfectly normal, was left in situ. The uterus, right tube and left tubo-ovarian mass were removed without difficulty, but in separating some widespread adhesions which surrounded the mass on the left side, the sigmoid was at one point torn through to the mucosa. This rent was repaired with a mattress suture of catgut.

The patient made an uneventful recovery.

Gyn. Path. No. 2376. The specimen consists of the uterus, the right tube and a left tubo-ovarian mass. The uterus is small and free from adhesions. Its mucosa is from

¹ Orthmann: Zeitschrift für Geburtsh. u. Gyn. Bd. xv, 1888.

² Friedenheim: Berliner klin. Woch., No. 25, 1899.

³ Doran: A System of Medicine, Albutt & Playfair. Trans. of the London Obstet. Soc., vol. xl, 1898.

⁴ Kaltenbach: Centralblatt, f. Gyn., 1889, p. 74.

⁵ Fabricius: Wiener klin. Woch., 1899, No. 49.

one to two millimetres thick, and apart from a slight superficial injection, appears normal. The right tube presents a few light adhesions, but is otherwise normal.

The uterine end of the left tube for a distance of three centimetres is moderately dilated and cystic, averaging about one centimetre in thickness. It then suddenly expands into a large cylindrical mass eleven centimetres long, three and one-half centimetres in diameter. This mass is of a pinkish or grayish color, covered with adhesions and somewhat yielding to the touch. The fimbriated end of the tube is firmly bound down to the ovary. The ovary is 5 x 4 x 3.5 centimetres in size and contains cysts from one to two centimetres in diameter. It is also enveloped in adhesions. The broad ligament is thickened and infiltrated. On cutting open the tube in its long axis a greatly distended canal is found, which is filled with a granular friable mass. This is not attached on all sides, but springs chiefly from the outer third and under surface of the tube, and the remainder of the tube wall forms a thin smooth capsule around the mass. On closer examination of the tumor it is found to consist of finely branched papillary outgrowths which, to a great extent, have coalesced, forming a more or less homogeneous mass.

The fimbriated end of the tube has been replaced by the neoplasm, and from it a papillary exerescence projects into a small cyst cavity in the ovary.

Histological examination.—The uterus and right tube are normal.

Sections from the margins of the tumor occupying the left tube show in the earliest portions some swelling of the epithelial cells and a tendency to become heaped up into little folds. Further on we see branching papillary outgrowths having a stroma composed of vascular connective tissue and covered with several layers of epithelium. In the multiplication of the epithelium, small gland-like spaces have here and there been enclosed. In most places the epithelial proliferation has been so great that the papillary outgrowths have become fused and the sections present masses of epithelium containing round and oval gland-like spaces, while scattered here and there throughout the field are longitudinal and transverse sections of stems of stroma (Fig. 2).

The epithelial cells on the whole are fairly uniform in size. The deepest layer is composed of low columnar cells, while the superimposed cells are polymorphous, becoming flatter on the surface. The gland-like inclusions are lined with cuboidal or flattened cells. The nuclei are large, oval or round, and have taken a somewhat deep diffuse stain. Mitotic figures are numerous and show various irregular forms. In favorable sections the papillary masses are seen to spring directly from the inner surface of the tube wall, corresponding to the folds of the mucosa; and at one or two points normal folds may be traced for a short distance, then merge into the tumor. In places the growth extends a short distance into the muscular coat in the form of solid nests of epithelium, or as small glands lined with one or more layers of cells (Fig. 3).

The portion of the tube invaded by the growth in places

shows considerable leucocytic infiltration, and the advancing margin of the tumor is generally bounded by a zone of round cells. The remainder of the tube is practically free from infiltration and presents no evidence of an old inflammation. The growth has invaded the ovarian stroma immediately adjacent, and the cyst-like spaces with which the tube communicates are lined in part with two or three layers of tumor cells. The other small cysts are merely dilated follicles and the stroma is normal. This tumor resembles in its finer structure the carcinomata of the uterine body, although its papillary formation is somewhat more distinctive than in most tumors of the uterus. This may be attributed to the fact that in the tube the outgrowths spring from the branched folds of the mucosa. On the other hand, inasmuch as glands are not normally found in the tubal mucosa and the glands invading the stroma are therefore entirely due to dipping down of the surface epithelium, the invasion is apt to be less general than in carcinoma of the uterus.

That this tumor is primarily tubal is evident in view of the following facts: ,

(1) The uterus is normal.

(2) The tube is large as compared with the ovary: ovarian carcinomata grow rapidly and attain considerable size before extension occurs.

(3) There is a definite relation between the papillary masses and the tubal folds, while the ovary merely shows invasion of parts adjacent to the tube and contains no papillary exerescences, excepting those projecting from the end of the tube.

(4) The mucosa of the tube is the site of the neoplasm, the invasion of the musculature being due to extension outward from the mucosa. In carcinoma of the tube, secondary to the ovary, the growth usually extends from the peritoneal coat inward and the canal may be normal or constricted, not dilated.

For more than a year after the operation the patient enjoyed excellent health. Then, however, she began to suffer from a feeling of discomfort in the lower abdomen, and as this persisted, an exploratory section was made in April, 1900, about two years after the first operation. A small oval mass about the size of an olive was found at the base of the left broad ligament, and a nodule the size of a small bean on the posterior surface of the bladder. These were dissected out, but several minute deposits infiltrating the pelvic peritoneum could not be removed. On histological examination the nodules removed proved to have the same structure as the primary growth. At the present time, a year after the second operation, the patient appears to be in good health.

Symptomatology.—The earliest manifestation of the presence of the disease is usually, a watery vaginal discharge, later becoming sanious. Hemorrhage is a variable sign: in five cases there was metrorrhagia, and in two others the menstrual flow was increased. Pain was present in the majority of cases, sometimes occurring before the appearance of the vaginal discharge, but more often later, and

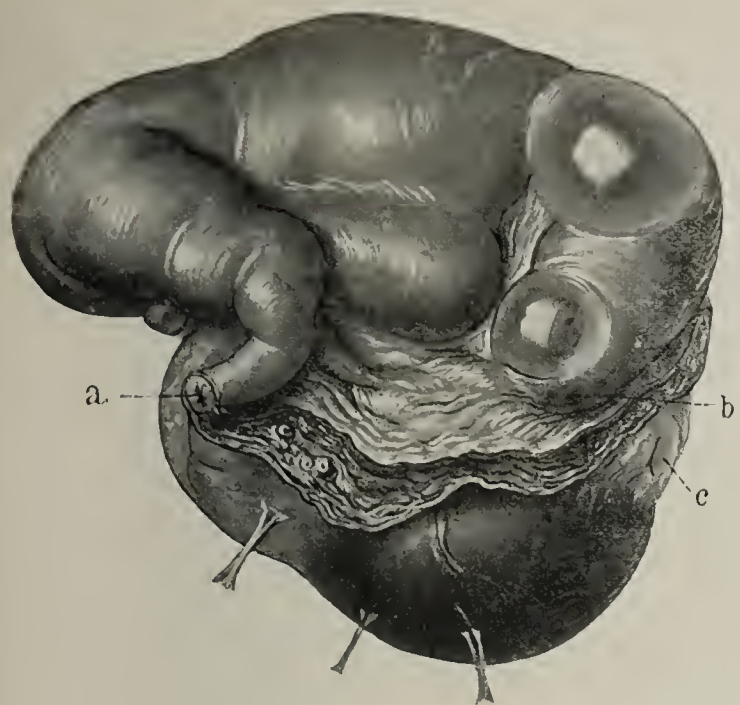


FIG. 1.—PRIMARY CARCINOMA OF THE TUBE. (Natural size.)—*a* is the proximal end of the tube and *b* the occluded fimbriated extremity. Near the uterus the tube is nearly normal in size, but rapidly enlarges until near the fimbriated extremity, it is 3 centimetres in diameter. At *c* are two subperitoneal cysts. The ovary *c*, contains a small cyst with dark colored walls. Attached to the under surface of the ovary are several adhesions.

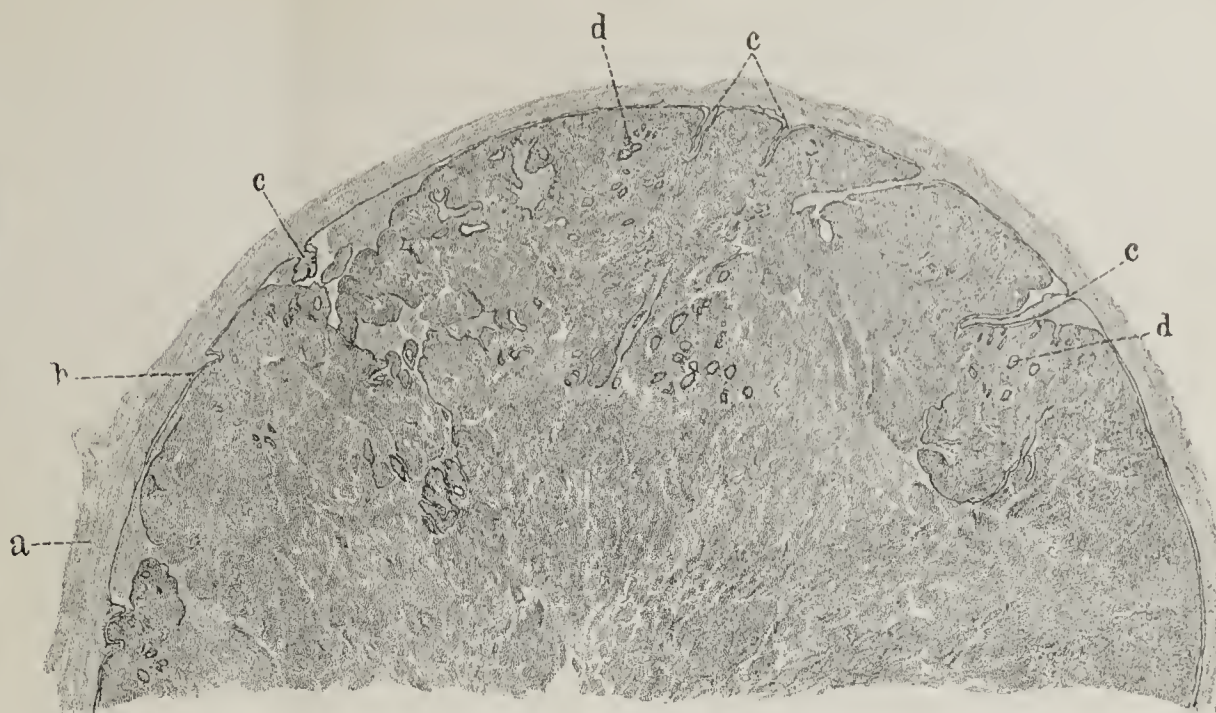


FIG. 2. TRANSVERSE SECTION THROUGH UPPER HALF OF THE CARCINOMATOUS TUBE. (6 diameters.)—The tube is fully five times its normal size. The wall, as represented by *a*, apart from being somewhat thinned out, is unaltered. *b* indicates the inner lining composed of one layer of cylindrical epithelium, in places somewhat flattened. The remnants of the bases of the folds are indicated by *c*. The lumen of the tube as indicated by the dark shade is completely filled with epithelial cells of the new growth. In many places these form a homogeneous mass, but at the points indicated by *d* assume a glandular arrangement.



FIG. 3.—ADENO CARCINOMA OF THE FALLOPIAN TUBE. (80 diameters.) The section is taken from the wall of the tube. *a* is the somewhat flattened but normal tubal epithelium. *b* a cross section of a normal fold and *c* the normal lining of a portion of a diverticulum from the lumen. Penetrating the wall of the tube and occupying nearly half of the field is carcinomatous tissue. The cells on the whole have fairly uniform nuclei, but here and there they are deeply stained and increased in size. At several points, especially in areas indicated by *d*, a distinct gland-like arrangement is demonstrable. Along the advancing margin of the growth there is considerable round cell infiltration, especially evident at *e*.

in some instances was only noticed a few weeks before the time of operation.

In the two cases reported by Roberts⁶ the patients experienced severe attacks of pain, followed by a profuse serous discharge with subsidence of the pain. These attacks occurred at intervals of about three months until operation was undertaken about a year after the first. Routier's⁷ patient gave a history of a similar attack. The presence of ascitic fluid was observed in only a few instances.

Age.—With four exceptions the disease appeared in the fifth or sixth decade. The youngest patient was thirty-five years of age, the oldest seventy years.

Number of pregnancies.—As will be seen in the following table, absolute or relative sterility was noticed in almost all cases. Data regarding the number of pregnancies were obtained in twenty-four cases. Two other patients were unmarried.

9	patients	had	no	children.
2	"	"	"	" but one miscarriage each.
7	"	"	1	child each.
2	"	"	2	children each.
3	"	"	3	" "

Diagnosis.—Carcinoma of the tube has not been diagnosed previous to operation, a diagnosis of ovarian cyst or of hydro- or pyosalpinx, having usually been made. The sudden onset of a serous or hemorrhagic vaginal discharge at or about the time of the menopause, and following a long period of sterility, at once suggests a new growth, as inflammatory disease usually becomes manifest in earlier life. If a pelvic examination reveals a mass in one or both fornices, and if the uterus is free from disease, there is probably a new growth of the ovary or tube.

Ovarian tumors are less often accompanied by a vaginal discharge and usually attain a greater size before giving rise to symptoms. The differential diagnosis however is sometimes impossible.

In determining whether we are dealing with an innocent papilloma or with a malignant tumor, the histological structure is chiefly to be considered. The simple papillomata present a branched stem of connective tissue, invested with a single layer of epithelial cells of uniform appearance, and not tending to invade the stroma. In the carcinomata the epithelial cells are polymorphous, are usually in several layers, and exhibit a tendency to invade surrounding structures.

⁶ Roberts: Trans. Obstet. Soc., xl, 1899.

⁷ Routier: Ann. de gyn. et obstet., vol. xxxix, 1893, p. 39.

ures. The papillomata, however, are always to be regarded with suspicion, as is shown in the cases of Kalténbach and Fabricius referred to above. In these the histological picture was that of an innocent tumor, but in each there was a recurrence.

The thin walls of the tube and its intimate relation to the broad ligaments favor extension of the growth beyond the limits of the tube. It is essential, therefore, when removing the tube to make a wide dissection of the pelvic connective tissue. It is advisable to remove the opposite tube also, as in twenty-five percent of the cases reported both tubes were affected, and in three or four others carcinoma developed later in the tube, which, as it appeared normal at the time of operation, had not been removed.

The prognosis, so far as can be determined from the small number of cases, is less favorable than in carcinoma of the body of the uterus. We find that three patients died as a result of the operation. In fourteen cases recurrence was noted in from two to eighteen months. Three were apparently well fourteen months, nineteen months and seven years later, respectively. The remaining cases were either lost sight of or were reported too early to furnish data as to ultimate results.

In the March number of the BULLETIN (after the above article had been sent to the publishers) a case of carcinoma of the tube was described by Dr. Le Count. The author emphasizes the importance of chronic inflammation as an etiological factor, comparing carcinoma of the tube to similar lesions following hyperplastic inflammation in other organs. I must, however, take exception to the writer's criticism of many of the cases previously reported. Most of these cases are carefully described in the original, and both the descriptions and illustrations clearly indicate the presence of carcinoma. For example, in the case reported by Fearne from Leopold's laboratory, Le Count apparently considers the growth to be a simple polypous hyperplasia. I have, however, had the opportunity of examining sections under the microscope and agree with Dr. Fearne's diagnosis.

In regard to the adeno-carcinoma of the uterus described by Cullen in his recent book, which Le Count declares is merely a case of polypous hyperplasia, it is evident that the latter writer has not studied the case carefully, as from the description it is seen that many portions of the growth show the typical picture of adeno-carcinoma. I have personally studied the case carefully and there is not a doubt as to its being a glandular carcinoma.

THE JOHNS HOPKINS HOSPITAL BULLETIN.

The Hospital Bulletin contains details of hospital and dispensary practice, abstracts of papers read, and other proceedings of the Medical Society of the Hospital, reports of lectures, and other matters of general interest in connection with the work of the Hospital. It is issued monthly.

Volume XII is in progress. The subscription price is \$1.00 per year. The set of twelve volumes will be sold for \$23.00.

LIPO-MYOMA OF THE UTERUS.*

BY J. H. MASON KNOX, JR., PH. D., M. D.

Clinical Assistant in Gynecology, The Johns Hopkins Hospital Dispensary.

Although fatty tumors are frequently found in many parts of the body, the presence in the uterus of a new growth, consisting in large part of adipose tissue is so rare as to lend some interest to the report of the following case:

The patient was a woman, aged 62, married, and the mother of thirteen children, the youngest 24 years of age. The labors had all been natural. She had had three miscarriages, the last twenty-six years before. Her menstrual history had been perfectly regular and normal. The menopause occurred twelve years previously. The family and personal history was excellent. She had always been in good health. The first indication of any abnormality occurred nine years ago, when the patient noticed a slight serous vaginal discharge. This passed away after some weeks and did not affect her general health. The discharge returned after an interval of over eight years, but again lasted but a short time, and was accompanied by no untoward symptoms. For two weeks before examination she had been bleeding moderately, but continuously. The discharge has never been offensive. On only one occasion did the patient suffer when she complained of a sharp pain like that during labor. Her appetite was good and the bowels were regular. There was slight increased frequency of micturition. The patient thought that she had gradually lost in weight. The heart and lungs were normal.

On abdominal and vaginal examination a large firm tumor was found connected with the uterus, filling the pelvis and extending almost to the umbilicus. Operation was advised and performed by Dr. H. A. Kelly and a large mass, including the uterus and appendages, was removed by the supra-vaginal route. The tumor was not densely adherent, and the operation presented no unusual difficulties, except for rather free hæmorrhage, which was finally perfectly controlled. The patient made a slow but satisfactory recovery and is at present, eighteen months after the operation, in fair health.

During the operation and indeed for some time afterward there was no suspicion that the mass did not consist of a simple large myomatous uterus. It was only in the routine examination of the specimen in the laboratory that its unusual structure was discovered. Hence it is to the pathological description that most interest attaches.

Pathological description (Gyn. Path. No. 3703).—The specimen consists of a uterus involved in a large tumor, both Fallopian tubes, a portion of the left ovary, and a cystic right ovary. The uterine mass is globular in form, regular in outline and approximately 15 cm. in length, 14 cm. in breadth and 18 cm. in its antero-posterior diameter. The surfaces are generally smoothly covered by peritoneum. On the left side, however, above the attachment of the tube, the surface is roughened by numerous tags of adhesions. The

tumor is firm and resilient in consistency. The uterine cavity is about 14 cm. in length. The mucosa of the anterior wall is glistening and is hardly 1 mm. in thickness. It is everywhere intact. That covering the posterior wall is much altered on account of the tumor which projects into it from behind. In some places many minute cysts are scattered throughout the mucous membrane, some of them being 2 mm. in diameter. In the upper part of the cavity is an area 4 x 4 cm., irregular in outline, sharply defined and very pale in color. At this point the mucosa is excessively thin and the tumor in the posterior wall almost comes in direct contact with the uterine cavity. In the lower part of the cavity is another pale area 9 x 9 cm. Here the mucosa is also thinned out but at numerous points it is still preserved, as witnessed by the small cyst-like spaces—dilated uterine glands. Situated in the upper part of the cavity is a sessile polypoid thickening 5 x 2½ cm. Here the mucosa varies from 1-7 mm. in thickness; some of the glands here are 1.5 mm. in diameter. The anterior uterine wall varies from .8 to 1 cm. in thickness and presents no abnormality. Occupying the posterior wall is a tumor mass somewhat globular in form (Fig. 1). It is approximately 10 x 13 x 10 cm. in size. On section the tumor to casual examination presents the appearance of myoma, but on more careful scrutiny is found to be markedly different. Traversing it in all directions are glistening bands between which are yellow soft looking areas. On scraping the cut surface distinct oil globules can be brought away, a thing that is never possible when an ordinary myoma is examined. The tumor itself presents no areas of breaking down. It is sharply defined from the surrounding uterine muscle, which varies from 3-5 mm. in thickness. At the point where the mucosa is pale-staining the tumor encroaches upon the uterine cavity to a marked extent and the mucosa here shows much atrophy.

Appendages.—On the right side the Fallopian tube is approximately 12 cm. in length, normal in consistency, and presents a uniform diameter of about 4 mm. Its surface is everywhere roughened and the fimbriated extremity is densely adherent to and occluded by the large ovary about to be described.

The ovary is converted into a lobulated mass, partly cystic, partly firm. The mass is somewhat bean shaped in outline and measures 8 x 5 x 4 cm. The inner pole is quite hard in consistency and on section is seen to be made up of dense fibrous tissue.

The harder portion merges into a small multilocular cyst which has a smooth, glistening surface with thin walls, and contains an iridescent yellowish fluid.

The cystic portion is divided into loculæ of various shapes and sizes by firm trabeculæ.

The several small pedunculated masses project into the cavity of the cyst.

* Read before the Johns Hopkins Hospital Medical Society, March 18, 1901.

The left side: Tube presents practically the same appearances as the right side. No induration; the surface is everywhere roughened, but a vestige of ovarian tissue remains in the broad ligament.

Microscopical description.—On microscopical examination the round tumor mass is found to be made up of large fat cells enclosed in a supporting substance composed of smooth muscle and connective tissue in varying proportions. The fat cells are generally round or oval, occasionally polygonal or irregular in outline from pressure upon each other. They vary in size from 5 to 15 times the diameter of a red blood corpuscle and appear, after hardening by the usual processes in which the fat is dissolved, like clear spaces (Fig. 2). The nuclei of these cells can frequently be made out as oval or rod-shaped bodies pushed to the periphery and often situated in an angle between several of the cells. The tumor is coursed throughout its extent by numerous bands of firm fibrous tissue which produce the lobulated appearance noticed in the gross specimen. This more solid material consists of round and spindle cells of the connective tissue type, having finely granular protoplasm and oval or spindle-shaped deeply-staining nuclei, together with a considerable quantity of intercellular substance. Intimately mingled with it in many parts of the growth are the longer cells of the smooth muscle type with rod-shaped, often wavy, nuclei. Considerable areas made up of connective and muscle tissue and containing no fat cells are met with throughout the tumor. The bulk of the tumor, however, is composed of groups of fat cells surrounded by irregular coarse bands of this firmer tissue. From larger bundles small filaments are given off which encircle the individual cells. These finest filaments apparently fuse with the cell walls so that numerous cell groups are met with in which the large globular fat cells appear to be in direct contact. In the larger bands of the supporting tissue are many larger blood-vessels, and numerous capillaries are present in the smaller septa. Many cells containing coarsely granular protoplasm, staining in eosin and having irregular deeply-staining nuclei (eosinophiles), are met with throughout the specimen, more particularly about the blood-vessels in the central portion of the tumor. Another form common in the growth are large round oval cells with a somewhat refractive protoplasm and rather pale staining nuclei. The cells of this variety, probably Mastzellen, are found between the processes of the connective-tissue cells. Nowhere in the specimen are fat droplets seen inside of either muscle or connective-tissue cells; that is to say, there is no evidence whatever of fatty degeneration. Occasionally more or less extensive areas are met with which stain homogeneously with eosin and are devoid of nuclei. These are areas of hyaline degeneration. The structure of the tumor is not materially altered as one approaches the periphery. The muscle tissue like that usually found in the uterine wall forms the immediate boundary of the mass on all sides, thus showing that the growth must have been interstitial in origin. In general, it may be said that the tumor is rather sharply demarcated from the surrounding tissue. In many

places, however, the muscle near the growth contains here and there scattered fat cells, and occasionally groups of them in the muscle render the transition to the tumor proper a more gradual one. The muscle cells themselves present no abnormalities. Where the pressure of the growth is most marked they are often arranged in rows parallel to the circumference of the tumor. Numerous blood and lymph vessels are present throughout the uterine wall. Here, too, there is no evidence of fatty degeneration. Beyond the upper and lower limits of the tumor the muscle wall is much thicker. This is particularly true inferiorly in the portion corresponding to the cervix where it is over 1 cm. in diameter and composed of irregularly arranged dense muscle bundles. As one ascends, however, over the protruding anterior face of the tumor the muscle bands become rapidly thin, frayed, and often difficult to distinguish from the connective tissue of the mucosa. Areas of hyaline degeneration are not infrequent in the muscle wall, particularly near the tumor. The uterine mucosa presents a varied picture. For the most part it is much reduced in thickness. The surface epithelium over the tumor is preserved in protected areas, where it consists of a single layer of low cylindrical ciliated cells. The stroma is rather dense and made up of the usual round and oval cells with darkly staining nuclei, and a considerable amount of finely granular intercellular substance. The uterine glands are exceedingly few in number throughout most of the mucosa. When found they consist of small irregular or simple tubules lined by cylindrical epithelium. They are situated for the most part quite near the surface. The mucosa which does not cover the projecting growth is also thinned. Here, however, many small uterine glands are present and the stroma is proportionally more cellular. The polypoid thickness (sessile polyp) is made up of loose connective tissue, consisting largely of round and oval cells. Scattered all through this area are numerous glands varying from simple tubules to cysts of considerable size. The former are lined by high cylindrical epithelium one cell in thickness. The epithelium of the more dilated tubules is lower, while the cells lining the larger cysts are cuboidal in type. Many dilated capillaries are present in this raised area, which thus presents the usual structure of uterine polyp.

Appendages.—Right side; tube. Sections taken at several points along its course fail to present any abnormalities in the structure of the tube. Near the cornu the epithelium lining the lumen is slightly wavy in outline, while toward the fimbriated extremity the mucosa is gathered into intricate folds and convolutions. The stroma and muscle layers appear normal. The outer surface of the tube is markedly roughened, as though torn away from adhesions.

Ovary.—The solid portion of the enlarged right ovary is made up of a rather cellular connective tissue, the cells are oval or fusiform, have deeply staining nuclei and are separated from each other by a large amount of finely granular protoplasm.

The walls of the multilocular cyst occupying the outer pole of the ovary are composed of a thin framework of con-

nective tissue lined by epithelium usually one layer in thickness, the cells varying in outline from a very low cuboidal to a high cylindrical type, according to the amount of pressure.

The small pedunculated masses projecting from the cyst wall into the lumen consist of a fibrous stalk covered by epithelium similar to that lining the remainder of the cyst. In several areas the epithelium appears to be more than one layer in thickness.

Left side: tube. Sections of the tube near the uterus and toward the fimbriae present the same appearances as those noticed in the right tube. The outer surface is likewise roughened.

Ovary.—But a small bit of the left ovarian tissue was found in the specimen. This is senile in type and made up of stroma cells rather closely packed together. No Graaffian follicles are seen. There are in places through the section coarse wavy bands of hyaline material, probably the remains of ruptured follicles. A few corpora fibrosa are present. At one point is a gland-like space nearly 1 mm. in diameter. This is lined by cells almost flat and containing oval deeply staining nuclei. At the opposite pole, possibly near the hilum, is a large amount of unstriped muscle fibre.

Consideration of the above findings leads to the conclusion that one is dealing with an actual new growth in the uterine wall composed of adipose tissue, the cells of which individually or in groups are surrounded by a marked increase in the smooth muscle and fibrous tissue elements in the proportion frequently found in so-called myoma uteri. The fact that no fat droplets are present in the cells of the firmer tissues and the absence of areas of softening in the tumor preclude the possibility that the condition may be due to a fatty degeneration, and suggests the unusual diagnosis of *lipo-myoma of the uterus* as being most properly descriptive of the specimen. That the right ovary is the seat of a small fibrous growth and a multilocular cyst, has of course no association with uterine tumor.

An examination of the literature at hand shows that but few, if any, cases of an exactly similar nature have been reported. As is well known, various degenerations of myomatous uteri are not uncommon and may be of such marked grade as to occupy a large part of the tumor.¹ Several cases have been recorded, chiefly by older writers, of tumors of the uterus which consisted of more or less homogeneous whitish or yellowish material, described variously as "Pure white fat,"² "Hard white fat insoluble in alkalies at boiling heat,"³ "Yellowish white glistening substance, containing crystals of cholestrin."⁴

These tumors, called by the authors "steomata," "insteo-

mata" or "cholesteomata," respectively, are likewise instances of degeneration and are not primary growths.

Meckel⁵ speaks of a tumor, involving the uterus described by Lobstein.⁶ The uterus was enlarged to the size of a seven or eight months' pregnancy by a "fatty tumor."

In 1853 Seegar⁷ described a case which seems to resemble the one here reported. It is briefly as follows: A widow, aged 53, had for a year suffered from rather severe metrorrhagia, not relieved by any internal medication. On examination a round mass, the size of a child's head, bluish in color and elastic in consistency, was found protruding from the external genitalia and held by a pedicle surrounded by muscle fibres. The pedicle was ligated and the mass removed. The mass "*consisted of a fatty tumor covered by a firm cellular membrane and coursed by fibrous tissue bands. Parts of the tissue were rather soft, others firm and poor in blood-vessels.*" The patient made a good recovery. No microscopic description is given.

In 1861 T. Smith⁸ presented to the Pathological Society of London a specimen removed by Mr. Paget from a woman aged 40. It consisted of a pedunculated mass the size of two fists united to the fundus uteri, but protruding between the labia. On section the tumor was made up largely of firm fibrous tissue but contained a small serous cyst and an "*adipose tumor, the size of a pigeon's egg, completely embedded in the substance of the larger tumor and surrounded by a fibro-cellular capsule, from which it was easily shelled out.*" No microscopic description is given.

A case of somewhat different nature was reported in 1880 by Schoinski.⁹ On examining a woman, aged 28, who had been married seven years, to find if possible the cause of her sterility, he discovered on the anterior lip of the cervix a small movable tumor which on pressure could be easily forced into the os, closing it like a valve. This was excised and "proved to microscopical examination to be lipoma." The patient became pregnant three months afterward.

It is evident, therefore, that an adipose tumor of the uterus is an exceedingly rare condition. A lipoma in this situation is also of interest because, as there is no fatty tissue whatever present normally in the uterus, a lipoma of this organ lends support in a limited way to the theory of Cohnheim as to the histogenesis of tumors, namely, that they arise from some misplaced embryological element.

I take pleasure in expressing my thanks to Dr. Kelly for the privilege of reporting the case, and to Dr. T. S. Cullen for much assistance in the interpretation of the specimen.

DISCUSSION.

DR. CULLEN.—I think this is a most interesting find. We have been making a systematic examination of all cases of

¹ Brunnings: Verhandlungen der Deutsche Gesellschaft für Gynäkologie, Bd. VIII, p. 348.

² Dressel, von Graefes und von Walthers, and Journal für Chirurgie und Augenheilkunde, 1853, Bd. XIX, p. 661.

³ Dr. Wm. Bush. Edinburg Medical and Surgical Journal, 1853, Vol. 79, p. 281.

⁴ H. B. Allen: Australian Medical Journal, 1879; n. s., 1, p. 536.

⁵ Handbuch der pathologische Anatomie, Vol. II, p. 311.

⁶ Sur l'organisation de la matrice, Paris, 1803, No. 15, p. 8.

⁷ Zeitschr. f. Wundärztze und Geburtshülfe, 1853, Vol. V, p. 24.

⁸ Transactions of the Pathological Society of London, 1861, Vol. 13, p. 148.

⁹ Chicago Medical Review, 1880, Vol. 1, p. 469.



FIG. 1.—Lipo-myoma of the uterus, natural size. The uterus has been longitudinally bisected. The left half is shown. The posterior wall is seen to be the seat of a large globular tumor, presenting on cross section the irregularly lobulated appearance described. This is due to the inclosure of fat cells by trabeculae of firmer tissue. The tumor is rather sharply demarcated from the surrounding uterine wall, which is everywhere thinned, the portion between the growth and the cavity being particularly affected. Near the superior limit of the cavity is a sessile uterine polyp seen in cross section.

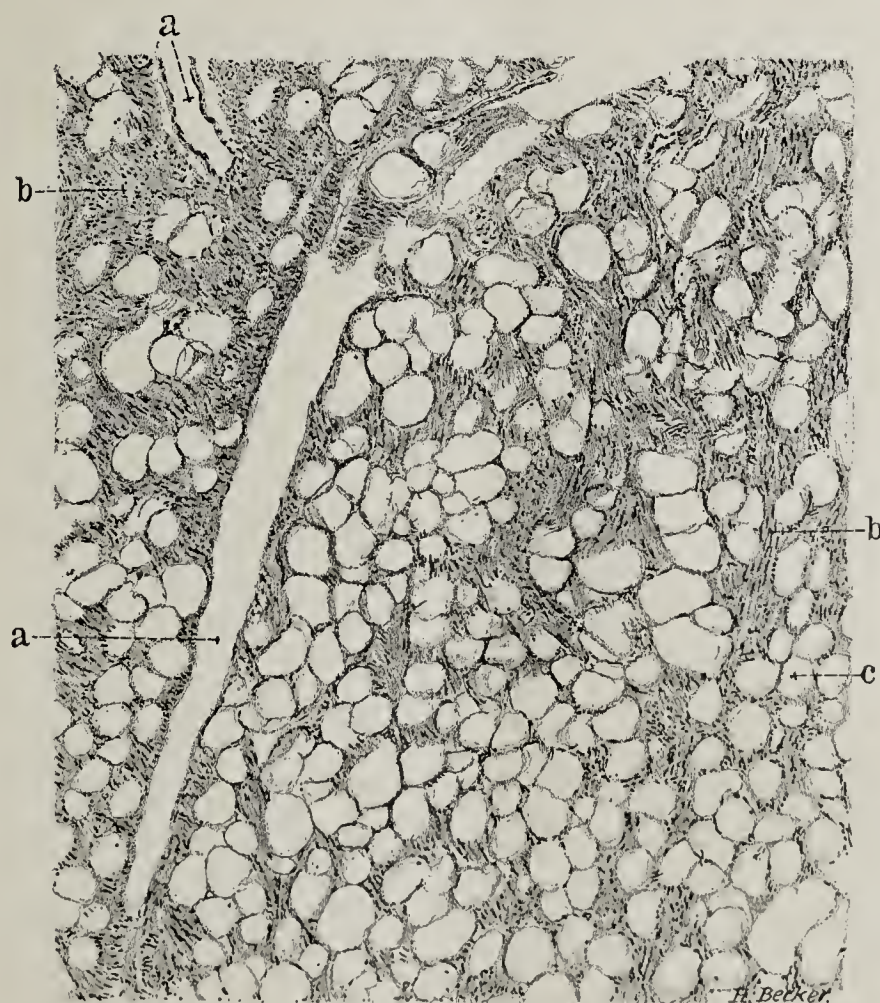


FIG. 2.—Lipo-myoma of the uterus (50 diameters). The section consists of a network, "b," composed of non-stripped muscle fibres and connective tissue in varying proportions. The interspaces, "c," are fat cells. At some points they are very abundant, at others isolated. "a" are blood vessels. Sections from all parts of the tumor present essentially the same appearances.

myomata and though over 600 specimens have been examined we have found but the one case of this character.

In nearly every myoma there is a hyaline degeneration in some part of the growth. This is usually diffuse, but in a certain percentage of the cases a large circumscribed area undergoes this degeneration. In the centre of such a block of hyaline tissue there is a gradual melting away, and we find nothing but a few threads of connective tissue and in the spaces between these free fat looking very much like melted

butter. In this free fat cholesterol crystals are frequently present.

A problem that is attracting a great deal of attention at present is the degeneration that takes place in myomata. It has been a mooted question for some time as to whether or not myomata can become malignant. We have in the laboratory at present at least three specimens in which the centres of myomata contained sarcomatous tissue.

CHOREA WITH EMBOLISM OF CENTRAL ARTERY OF RETINA.

A SHORT REVIEW OF THE EMBOLIC THEORY OF CHOREA.

BY HENRY THOMAS, M. D.,

Clinical Professor of Nervous Diseases, The Johns Hopkins University.

The subject of this communication is a young girl in apparently perfect health, except for slight choreic movements, which involve the right arm and leg, and very slightly the face. A closer examination shows, however, that she is suffering from the effects of an extremely rare and interesting complication of chorea, viz.: Embolism of the central artery of the retina. An abstract of the history, taken in the Neurological Dispensary of the Johns Hopkins Hospital, is as follows:

Dis. Nerv. System, No. 11,722.—Elizabeth C., age 16; sewing machine worker, was admitted to the dispensary Jan. 31, 1901, complaining of nervousness.

The *family history* is unimportant, except that one of her three brothers has had rheumatism, and that her mother, at the age of 51, is suffering from a facial tie of the left side. Other than this there is no history of any nervous disease in the family.

Personal History.—The patient is the fifth child of six; her birth was normal. She was healthy as a child, and developed normally. She had measles and whooping-cough, but no other infectious diseases and has never suffered from rheumatism. She began to menstruate at fourteen, and has since been regular.

For the last three years the patient has been working in a factory at a sewing-machine, which is run by power. She has been industrious and ambitious and her mother thinks that overwork may be accountable for her present trouble; at least neither mother nor daughter can think of any other possible cause.

Present Illness.—About six or seven weeks before she came to the hospital, an unsteadiness in the movements of her right hand attracted attention. This was noticed at table, and while the patient was at work in the factory. There was no change in her disposition, but a certain awkwardness developed in her speech. The movements also involved the legs on the right side.

The patient says that she has been unable to see with the

left eye since the trouble began; but unfortunately she can give no definite account as to exactly when this blindness occurred. She says that it came on suddenly, and when she discovered the defect it was as complete as it is now. She also thinks that she was first conscious of it at about the time she began to be nervous. I have been unable to get a more definite history from the other members of the family.

Examination.—At the time of the first visit, the patient showed a mild grade of choreic movements which were limited to the right arm and leg, with occasional movements of the face. Speech was not noticeably affected. She was slightly anemic—hemoglobin being about 70%. Examination of the heart by Dr. Jacobs revealed a slightly dilated heart, with a rough blowing systolic murmur, heard at the apex.

Vision in the right eye was normal, but that in the left eye was absolutely nil. The right visual field was normal both to form and to colors. The ophthalmoscopic examination showed optic atrophy of the left optic nerve with markedly contracted arteries. The right optic nerve was normal. The pupils were equal, and were between 5 and 5½ mm. in diameter. In a dim light, however, the left pupil was slightly larger than the right. The right pupil reacted actively when light was thrown into that eye, but not at all when light was thrown into the left eye. The left pupil contracted when light was thrown into the right eye, but was immobile when the light was thrown into the left eye; that is, the right pupil reacted to direct light, but not consensually, whereas the left pupil reacted consensually but not directly. When the patient endeavored to fix an object brought close to the face, both eyes converged and both pupils contracted. When the right eye was closed the patient was unable to make the effort to accommodate with her left eye.

When first examined, it appeared that the left pupil dilated and contracted synchronously with the choreic jerks; upon the second visit, however, the right eye being bandaged and the left pupil being carefully watched, this observation

could not be confirmed. Nor was it possible to discover any choreic movements of the external muscles of the eye, although the ball showed the unsteadiness so often seen in blind eyes.

The case presented the typical picture of unilateral chorea of slight grade, with involvement of the optic nerve, and the probable diagnosis of embolism in the central artery was made, although at the time I did not recall having heard of any similar case. The patient was referred to Dr. Reik for ophthalmoscopic examination, and he has kindly made a careful examination, and will describe the condition which he found. He confirmed the diagnosis of embolism of the central artery of the retina.

The eye complications of chorea are not very numerous. Muscles of the eye-ball are at times, though rarely, the seat of choreic movements. Gowers¹ calls attention to the fact that the movements may be unequal in the two eyes, and so cause diplopia. This being transient, is not often complained of. The pupils have been described as dilated, and as reacting sluggishly or not at all to light. This statement which is an old one, has not been confirmed by later observers, who state that the pupils are usually normal in their size and action. Choreic movements of the iris, such as I at first thought were present in the case described above, have been described by Dr. H. B. Scheffeld,² who observed in a choreic girl of 10 the most remarkable movements of the pupils. They would dilate as well as contract repeatedly within one minute. At times they were the size of a pinhead and at times they were dilated *ad maximum*. He confirmed the occurrence of these movements repeatedly during the attack of chorea. They disappeared when the patient recovered.

Gowers³ refers to optic neuritis as not very uncommon. Usually slight. He says, however, that twice⁴ he has seen it of such a high grade of intensity as to suggest the presence of a brain tumor. It subsides with the chorea.

Atrophy of the optic nerve is said to have been observed, and Schmidt-Rimpler⁵ refers very briefly to such a case. These are probably cases following embolism of the retinal artery or are associated with some disease other than chorea.

Embolism of the central retinal artery is the complication which interests us particularly at this time. When referred to at all by the authors it is always spoken of as being extremely rare. Gowers, in his Medical Ophthalmology, says that there have been only two cases (Swanzy and Forster), and in his text-book he refers to only one—but this, a third case, that of Sym. Knies⁶ speaks of the cases of Swanzy

and Sym. Schmidt-Rimpler⁷ has also no new cases to cite, and simply mentions these cases referred to by Gowers.

Swanzy,⁸ besides his own case, gives references to the cases of Benson and Leber.

I have been unable to add very materially to this list in my somewhat hurried view of the literature. It was pointed out long ago by Trousseau, in his Clinical Lectures,⁹ that impairment of sight had been observed by several authors, and he, himself, records a case. This impairment of sight, which he says, is probably due to paralysis of the retina is an accident excessively rare. The first well-reported case, as far as I have been able to find, was that of Swanzy, which is so generally referred to. On account of the great interest of these cases I shall give a short abstract of this case and of the others which I have collected.

DR. SWANZY'S CASE.¹⁰—Lizzie, ———, age 10. Seen 16 days after onset. Patient noticed upon waking in the morning following a long day of sight-seeing that she could not see with the left eye. Choreic movements, more marked on the left side, made their appearance at about the same time. The ophthalmoscope revealed the typical picture of a recent embolism of the central artery. No heart lesion was found. Optic atrophy followed. The chorea disappeared.

DR. LEBER'S CASE.—I. H. Leber¹¹ says: "I have seen a single example of one-sided atrophy of the optic nerve in connection with chorea which was apparently due to embolism of the central artery. The patient was a girl eight years old, who had suffered from chorea for a number of years. The loss of sight had followed very suddenly a few months previous to the examination. Well-marked, one-sided atrophy of the nerve was found, the vessels being of very small caliber. Amblyopia Amaurotica existed. The second aortic sound was of an increased intensity, which only strengthened the theory of an embolic process being the causative factor in the optic atrophy.

DR. BENSON'S CASE.¹²—James Jackson, age 21. Rheumatic fever when 17; chorea at 18; recurrence when 19 and again when 20. When 21, the day before admission, he became progressively but quickly blind in the right eye; he could not see light. In about ten minutes the sight improved in the lower field. When examined, there was complete loss of the upper half of the right visual field. The ophthalmoscope showed the characteristic picture of embolism in the inferior division of the central artery. No lesion of the heart could be discovered. In 2 months the ophthalmoscopic picture was normal.

DR. BALL'S CASE.¹³—Boy, age 15. Maternal grandmother

¹ Trans. Ophth. Soc. United Kingdom, 1884, iv, 306.

² Am. Med. and Surg. Bull. New York, 1896, vol. x, p. 373. "A case of Chorea Minor, involving also the ciliary muscles."

³ Med. Ophthalmoscopy. Third edition, 1890, p. 198.

⁴ In the second edition of his Diseases of the Nervous System, 1893, vol. ii, p. 604, he states that he has seen but one such case.

⁵ Nothnagel Special Path., etc., 1898, vol. xxi, p. 46.

⁶ Relations of diseases of the eye to general diseases. New York, 1895, p. 240.

⁷ Loc. cit., p. 286.

⁸ System of Diseases of the Eye. Norris and Oliver. 1900, vol. iv, p. 630.

⁹ Bazire's Trans., p. 402.

¹⁰ H. R. Swanzy, Ophthalmic Hospital Reports, vol. viii, p. 181.

¹¹ Graefe und Saemisch. Handbuch der Augenheilkunde, 1877, vol. v, p. 870.

¹² The Ophthalmoscopic Review, 1886, vol. v, p. 1.

¹³ Transactions of Clinical Society of London, 1887-8, vol. xxi, p. 279.

and two brothers had rheumatism. Patient had not suffered from rheumatism. 1st attack of chorea 8 years before, since which he has never been quite free; worse for the six months before examination. Five days before he was seen, he noticed in the morning a darkness before the right eye; he could only see the upper part of objects with that eye. The fundus was normal with the exception of an arterial branch which was constricted, especially at its origin. There was haziness of the retina in the distribution and of the adjacent section of the optic disk. The apex of the heart was in its normal position, and there was a soft systolic apex bruit.

DR. SYM'S CASE.¹⁴—G. S., boy, age 17. Had been well up to his seventh year, when he had chorea, which was not very severe. Was in the Infirmary and doing well; when walking one morning in the ward he felt a sudden mist come over the right eye. He has never seen out of it since. Examination showed left eye normal—right eye absolutely blind. In endeavoring to fix a near object, the right eye did not converge.

Right eye did not contract to light, but did so in sympathy to left. The right optic nerve was atrophied. There was a presystolic murmur and a reduplication of the second sound. In speaking of the rarity of these cases, Sym said that "Dr. Argyll Robertson informs me that a few years ago he saw a precisely similar case—that of a young lady in whom atrophy of one optic nerve succeeded a severe attack of chorea."

FÖRSTER'S CASE.—"The other case was recorded by Förster, but was not seen until some time after its occurrence. The patient, a child, had suffered from chorea for some years and during the chorea, had lost the sight of one eye. The disc was atrophied and the arteries very small."

Besides these cases, I have no doubt others could be found in which the embolism occurred at a late period in cases of chorea, followed by heart lesions. For instance, one of the cases pictured by Frost in his beautiful Atlas, "The Fundus Oculi,"¹⁵ is that of a woman, 50 years old, who had had rheumatism when nine years old and several attacks of chorea between 11 and 15, rheumatic fever at 28 and again at 49, and embolism of the central artery at 50. But such cases can hardly be considered as complications of chorea.

Ophthalmologists are not in accord on the subject of embolism of the central artery, and a number of excellent observers believe that many of the cases classed under this head are examples of thrombosis. Their objection is that no source for the emboli can be found, while the causes which favor thrombosis are present. These objections can not be urged against the cases occurring in chorea, especially when there is a demonstrable lesion of the valves of the heart.

Not only do the authors who describe such cases consider them dependent upon emboli, but with hardly an exception they all point out the support which they lend to the theory

of the embolic origin of chorea. Swanzy,¹⁷ writing very lately, in reference to this point, says: "Possibly therefore the embolic theory of chorea may yet be found to be more tenable," at least for some cases of that affection, than Gower believes and Knies¹⁸ is still more positive with the statement: "These two cases (Swanzy and Sym) demonstrate the development of chorea by multiple emboli; however this is not the sole cause of the disease."

The embolic theory of chorea is of great historical interest, and as it is so little referred to in modern text-books, a brief review may be of value.

The association of chorea with rheumatism and lesions of the heart was noticed in the 18th century, but particular attention was first drawn to it about the middle of the last century. Roger, in France, 1866, went so far as to state that rheumatism, chorea and endocarditis were all manifestations of the same poison. In England, where a great deal of attention had been paid to chorea and to this association, the relation between these conditions had received another explanation. Kirkes¹⁹ advanced the theory that the relation was not between chorea and rheumatism but between chorea and valvular heart disease excited by rheumatism. He considered that chorea usually follows the heart disease, and he said: "And I now believe that whenever chorea occurs in association with acute rheumatism, the valves of the left side of the heart are inflamed and therefore the association is not between chorea and rheumatism but between chorea and valvular heart disease excited by rheumatism. . . . We can readily understand that the blood in such cases often previously unhealthy from rheumatic poison and now rendered still more impure by the introduction of inflammatory products and fibrinous particles from the diseased valves, is calculated to disturb very materially the functions of the various organs through which it circulates." Later he says: "Partly by the mere circulation of morbid blood through the nervous centers, partly also perhaps by temporary obstruction in the minute capillaries, occasioned by fibrinous particles arrested therein, the irritation leading to the development of chorea or other analogous phenomena may be accounted for."

About this time great interest was aroused in the physiology of the brain. Broca had demonstrated that speech was located in a definite part of the brain cortex. Hughlings Jackson had deduced from his clinical observations that there must be some sort of localization of the movements in the brain. The cortex had, as yet, not been proved to be excitable by electric stimuli, so it was thought that this localization of motion was to be looked for in the so-called sensory-motor ganglia, and particularly in or about the corpora striata. The fact that chorea so often affected the muscles of one side of the body, and that when it was bilateral, it was usually unequal, pointed to the brain as being the seat of the

¹⁴ Edinburgh Med. Jour., 1888, March, p. 811.

¹⁵ Gowers Med. Ophthalmoscopy, p. 198.—I have been unable to trace it.

¹⁶ London, 1896, pl. xli.

¹⁷ Norris and Oliver's System, 1900, vol. iv.

¹⁸ Loc. cit.

¹⁹ Med. Times and Gazette, 1863, vol. i, pp. 636-662.

lesion, and Hughlings Jackson,²⁰ Broadbent,²¹ Russell Reynolds, and others assumed that it was in or about the corpora striata that the primary seat of the disease was to be sought, and adopting Kirkes' view, they taught that multiple emboli were the most probable cause. This theory, supported by such men, carried great weight, but it was never generally accepted. For it was pointed out that in the cases of chorea which came to autopsy emboli could only rarely be demonstrated, and in cases where emboli were found after death, chorea had very seldom been present. Dickenson²² gives most interesting data on this subject after detailing the anatomical findings in seven cases of chorea.

The embolic theory appeared, however, to receive a certain experimental confirmation from the work done by Money,²³ who succeeded in producing in the lower animals movements which could not be distinguished from those of chorea. He did this by introducing into the circulation minute particles that could be easily recognized by microscopical examination. He found that the choreic movements resulted only when the emboli lodged in the capillaries of the upper part of the cord. When the brain was the seat of the emboli, many other "forced movements," but not those of chorea. These experiments, he believed, demonstrated that choreic movements could be produced by capillary emboli, but he did not argue from them that human chorea depended upon a disease of the spinal cord. Against this there were too many well-known facts which spoke definitely for the brain being the seat of the process. He spoke of continuing these experiments upon monkeys, but of these I have seen no report. In the interesting discussion of Money's paper,²⁴ Hughlings Jackson, Broadbent and others took part. Hughlings Jackson and Broadbent referred to their former views and seemed to think that these experiments were to a certain extent confirmatory of them. Dickenson²⁵ again reviewed the subject in the light of Money's experiments, but was unable to find any confirmation for the embolic theory of chorea from the pathological reports of St. Georges Hospital and the Hospital for Sick Children.

This and similar investigations, as well as certain well-known clinical characteristics of chorea, spoke so strongly against the theory, that it was practically abandoned. Gowers speaks of it as of merely historical interest.

It is not my intention to speak in detail of the current theories that have been advanced in the endeavor to explain the etiology and symptoms of chorea. They will be found very fully discussed in the late monographs on the subject, especially the one by Wollenberg in Notknagel's series.²⁶ But it may be of interest to point out that our views in regard to

the localization of the morbid process upon which choreic movements depend, follow directly upon our physiological belief. This must be so, for, as yet, pathological examinations have given us no definite data. Hughlings Jackson, Broadbent and others placed the lesion in or near the corpora striata or optic thalami, for at that time it was believed that the movements of the body were coordinated in these structures. As our knowledge of the cortex increased, it was demonstrated that coordinate movements could be elicited by irritation applied to special areas of this structure and that the destruction of these areas caused paralysis of the movements. These most interesting discoveries directed the attention of the whole medical world towards the brain cortex almost, one is tempted to say, to the exclusion of the rest of the brain. Every disease in which abnormal muscular movements were a prominent feature was believed to depend upon some lesion of the motor cortex. Choreia was among the others, and at present the general opinion is that the wild movements of the disease depend upon some morbid process acting on the cortex. Of late, however, physiologists have been calling attention to the very important part that sensory impulses play in the production of coordinate movements, and to the extreme complexity of the mechanism underlying such movements. Destruction of many parts of the nervous system other than the so-called motor tracts causes marked disturbances. Ataxia, due to disease of the sensory spinal roots and of the sensory path within the central nervous system; experimental paralysis, caused by cutting the afferent roots of a limb; the forced movements and paralysis following destruction of parts of the cerebellum, may be mentioned as examples.

It is quite conceivable that an irritative lesion, or indeed, a destructive lesion, acting on some one or more of these structures might cause the involuntary incoordinate movements so characteristic of chorea. But at present the facts are too few to permit of anything more than a suggestion as to the direction in which the lesion is to be looked for. There are certain things that make it difficult to believe that it is a disease of the cortex, especially the motor cortex, that is responsible for the movements in chorea. That irritative lesions of this structure are followed by abnormal muscular movements, is one of the best established facts in pathology of the nervous system; but the movements which have been proved to follow lesions of the cortex are not at all like those seen in chorea, but follow the general type of epileptic convulsions; and, on the other hand, it is remarkable how very uncommon it is for such convulsions to occur in chorea, even in the most intense cases. In the slow systemic degeneration of the motor path, as it occurs in progressive central muscular atrophy (amyotrophic lateral sclerosis) incoordinate muscular movements, either voluntary or involuntary, are not present, the well-known fibrillary tremor being of quite a different character. In certain cases of hemiplegia and diplegia in children, movements develop which are, at times, quite like those seen in chorea, and this would seem to lend force to the belief in the central origin of chorea, or at least

²⁰ Edinburgh Med. Jour., October, 1868, p. 294. Med. Times and Gazette, 1869, March 6.

²¹ Brit. Med. Jour., 1869, April 9, 345 and 369.

²² Medico-Chir. Trans., London, 1876, p. 1.

²³ Med. and Chir. Trans., London, 1885, vol. lxxviii, p. 277.

²⁴ Lancet, 1885, vol. i, p. 985, and in other journals.

²⁵ Lancet, 1886, vol. i, p. 10.

²⁶ Specielle Path. u. Therapie, Bd. xii, ii, Th. 3d Abth.

to the view that the motor path is involved. In some such cases, however, lesions have been found in the central ganglia, especially in the optic thalamus, and it is upon these that most authors believe that the post-paralytic chorea depends, and not upon lesions of the pyramidal tract.

Therefore, if these cases have any significance in explaining Sydenham's chorea, they point to some structure other than the motor cortex and the fibres leaving it, as being at the root of the trouble—possibly to the optic thalamus. One is tempted to assume, as did Hughlings Jackson and Broadbent long ago, although for quite different reasons, that the morbid agents underlying chorea act upon the central ganglia. Of the functions of the corpora striata practically nothing is known, but anatomical investigations make it seem very probable that in the optic thalamic sensory or afferent impulses are rearranged before being distributed to the cortex. It is easy to imagine that a lesion here could so disarrange the afferent impulses passing through it that the voluntary movements depending upon these impulses would be incoordinated or, indeed, that involuntary incoordinated movements might result. But, as I said before, the anatomical basis which underlies coördinate muscular movements is extremely complex and is, as yet, but partially known. It therefore seems but of small value at the present time to advance any theory as to the seat of the morbid process of chorea.

I cannot resist the temptation, however, to express my conjecture that when the lesion is found, it will be on the afferent rather than on the efferent side of the motor mechanism.

In regard to the morbid agent, I have but little to say. The objection to the embolic theory seems so strong in the light of our present knowledge, that I do not see how it can be held. The cases of embolism in the central retinal artery during an attack of chorea demonstrate that such emboli are at times present in the circulation of choreic patients, which is no more than would be expected when we consider how common endocarditis is in association with this disease; but they cannot be made to prove that the disease depends upon emboli in some other part of the brain—indeed, what is strange is the great rarity of emboli of all kinds in chorea.

The belief which is common now differs but little from that held in the early part of the last century, when the relation between chorea and rheumatism was so strongly urged. It was then thought that joint affections, endocarditis and chorea were all different manifestations of the poison upon which inflammatory rheumatism depends. Now we would say that the poison is similar to the rheumatic poison and so avoid the definite statement that it is the same Wollenberg, who calls the disease infectious chorea, thinks that it practically always follows some form of rheumatic infection, and bears to this the same sort of relation that the paralysis following diphtheria does to the diphtheritic infection. He speaks of it as a meta-rheumatic process.

DISCUSSION.²⁷*Ophthalmoscopic Appearances.*

DR. REIK.—Through the kindness of Dr. Thomas I had the privilege of seeing this patient and the opportunity of sketching the ophthalmoscopic appearances. Perhaps a word in explanation of, and apology for, this colored sketch should be given before passing it around. The members of this Society are so accustomed to the artistic work of Brödel and Becker that one naturally hesitates to exhibit the efforts of an amateur. The endeavor to illustrate some of the main features of the ophthalmoscopic picture of this eye has, however, I hope, been sufficiently successful to serve its purpose of aiding you to understand the conditions described.

You will observe that the central retinal artery, as it emerges from the central canal is very small and its branches appear like fine red lines as they spread out in the retina. Their lumen has not been entirely obliterated, although the contraction has reduced them to almost capillary dimensions. The vessel walls are distinctly recognizable for a short distance beyond the disc margin by the delicate white lines bordering the narrowed red column. The superior, nasal and temporal branches can be traced quite to the periphery and, after passing the first subdivision, it is noticeable that they increase somewhat in size; possibly the result of anastomosis. The inferior nasal branch is lost about 3 or 4 mm. from the disc, being entirely invisible beyond that point.

The veins are somewhat smaller than normal and appear to be slightly smaller on the papilla than towards the periphery.

The optic disc shows a well marked atrophic condition and its sharply defined edges are surrounded by an irregular ring of choroidal pigment. The macular area is of deep red color and the fovea is seen as a bright, but very minute, yellowish spot. Between the macula and the disc, close to the former, is a narrow semicircle of hazy white retina, with several white dots to the temporal side. Pressure on the globe fails to produce either arterial or venous pulsations. The eye is absolutely blind. Taken in full the picture is a striking one and typical of an obstruction in the central artery of the retina.

The complete blindness which results suddenly from an obstruction of this vessel is said to be permanent even though the occlusion be but brief and be soon followed by a restored circulation. A few hours only suffices to bring about the functional death of the retina. If seen shortly after the embolism occurs the arteries are seen as narrow white bands, or as thin red lines on the disc, which are not visible far beyond its margin. Within a few hours the retina becomes generally hazy, and, in its thickest portion, between the disc and macula, of a denser fluffy-white character, the result of edema or possibly post-mortem changes. The macula itself appears of a deep red color in marked contrast to the pale surroundings. This has been said by some to be

²⁷ Meeting of the Johns Hopkins Hospital Medical Society, February 18, 1901.

due to hemorrhage, but it is more likely only the appearance of the deep red choroid seen through the retina at this point and contrasted with the pale fundus.

At a later stage the vessels again become visible and are seen to carry a thin stream of blood; the obstruction has either been incomplete, the embolus has shrunk and allows some blood to pass, or a collateral circulation has been established. It has been generally held that the retinal is a terminal artery and that anastomosis with the choroidal or ciliary systems is impossible. Leber was unable, by injection experiments, to demonstrate any connection between these systems and the establishment of a collateral circulation has never been proven *post-mortem*, still certain clinical evidences seem to support the view that it may occur. For instance, the arteries, as in this case, may appear larger in the periphery than towards the disc, and in some cases observed by Hirschberg and others, the blood current has been seen to move towards the disc. Such a collateral circulation can only come from the short ciliary arteries which sometimes send branches, the cilio-retinal arteries, to the temporal side of the disc, or from the long anterior ciliary vessels in the sclerotic and choroid. In this case there are no such vessels visible on or near the disc, but the distal parts of the superior retinal arteries do appear to be somewhat larger than their proximal ends.

DR. RANDOLPH.—I was much interested in Dr. Reik's description of this case, particularly in regard to the cherry-red spot in the neighborhood of the macula. I think the most reasonable explanation of it is to be found in the condition of the retina at that point. In the region of the macula lutea, the retina is thinner than anywhere else and we can easily understand that the red color of the choroid seen through this thinner area would be more emphasized at this point than elsewhere. This is the case in the normal eye. I think, as Dr. Reik said, that it could not be due to hemorrhage. One of the particular points of difference between embolism of the central artery and thrombosis of the central vein is the absence of hemorrhages in the former affection. In thrombosis hemorrhages are always seen. I think, then, the red spot is due to the thinner retinal tissue in this region and this color is of course much accentuated by the anemia of the surrounding retina.

DR. OSLER.—It is surprising that embolism does not occur oftener in chorea; perhaps there is no disease in which endocarditis occurs more frequently. Some 6 or 8 years ago I took the trouble to go over 73 comparatively recent autopsy reports in chorea cases, in 67 of which endocarditis was present and yet embolism is certainly rare. In one of the five autopsies in chorea I found a spot of embolic softening in the corpus striatum.

VOLVULUS OF MECKEL'S DIVERTICULUM WITH RECOVERY AFTER OPERATION.

BY WILLIAM J. TAYLOR, M. D., Philadelphia.

Attending Surgeon to St. Agnes' Hospital and to the Orthopedic Hospital and Infirmary for Nervous Diseases. Consulting Surgeon to the West Philadelphia Hospital for Women.

A little girl, aged six, was admitted to St. Agnes' Hospital late in the afternoon of Wednesday, April 11, 1900. The family history was negative, except that a brother had been operated upon for an acute appendicitis.

All her life long she has been subject to occasional attacks of abdominal pain which had always been relieved by a purgative. On April 9, 1900, she was seized with sudden and acute abdominal pain and was under the care of her family physician who was unable to open the bowel by ordinary measures. This condition persisted, and she was admitted to the hospital on the afternoon of April 11, forty-eight hours after the beginning of the attack. I saw her within an hour, when she had the appearance of being extremely ill with a temperature of over 100° F., intense pain and marked rigidity of the abdominal muscles, and a rapid and very weak pulse. Presuming from the history and her physical condition that I had to deal with an attack of acute appendicitis, and the rigidity of the abdominal wall being such that I could not make a careful examination, she was immediately etherized

and the abdomen opened by a small incision in the right side. Introducing my finger, a tense rounded mass was perceived, filling the whole of the right side of the pelvis, resembling somewhat an enormously distended intestine, and upon enlarging the wound I could see a dark, almost black, ill-smelling mass. The intestines were so much distended that I was obliged to open the ileum at one place to get rid of a large amount of gas and liquid feces before I could bring the intestines under control. This I consider a much safer proceeding than evisceration, especially in young children who bear such manipulations badly. I then enlarged the wound and, after some difficulty, delivered a dark-colored, almost gangrenous, cystic tumor, which upon careful investigation proved to be a Meckel's diverticulum, springing from the wall of the ileum farthest away from the mesentery and about fourteen inches from the cæcum. One inch from the intestine proper, the pedicle of the diverticulum had twisted upon itself three complete turns, thus cutting off the circulation and causing it to become gangrenous. The distended end of the diverticulum was about the shape of a potato with a pedicle not larger than a lead pencil at the point where the twisting occurred, and was entirely free in the

¹ Read before the Johns Hopkins Hospital Medical Society, February 18, 1901.

abdominal cavity, except at its point of attachment to the ileum. There was no evidence of a cord-like remains of the diverticulum nor of the omphalo-mesenteric vessels. There were no adhesions of any moment holding the cyst, if it can be so called, in place, but the whole of the pelvis was filled with it. The rough measurements of this mass were $3\frac{1}{2}$ inches long by 2 inches wide. This small pedicle was grasped with a clamp forceps, and it was then cut away from the intestines through sound tissue, the wound invaginated, and closed with a double row of Lembert sutures. It was necessary to almost completely eviscerate the child before this mass could be delivered through the abdominal wound. The intestines were much congested and at several points were covered with patches of lymph and several coils were glued together by adhesions. The glands in the mesentery were



Photograph of Meckel's Diverticulum, natural size. Showing the pedicle grasped by clamp forceps.

enlarged and hard, several being the size of a lima bean, but the majority were not larger than a pea. In view of the gangrenous condition of the cyst, a small rubber drainage tube was introduced after free flushing of the abdominal cavity with a saline solution. The pedicle was so softened that in examining the diverticulum after its removal, its wall burst and quite an amount of its contents—which consisted of fluid fæces—escaped. This photograph taken by flash light was made within a few minutes after its removal and shows admirably both its size and appearance, although, owing to the escape of some of its contents, as I have just stated, the distension of its walls is not so great as at the time of its removal.

The greatest haste possible with accurate work was employed during the operation which produced profound shock.

Reaction occurred very quickly, however, and convalescence was rapid and uneventful. She was discharged from the hospital at the end of three weeks.

This case was absolutely unique in my experience, as from the history, the symptoms, and the examination of the child before operation, I had no doubt but that my diagnosis of an acute appendicitis was correct, while she was too ill and her symptoms too urgent for any elaborate physical examination. At first I was utterly at a loss to explain the cystic mass which I could feel within the pelvis and, indeed, I suspected it to be an ovarian cyst which had become strangulated. The cause or mechanism by which the diverticulum became twisted upon itself is quite beyond my explanation, but it is possible that the peristaltic movements of the intestines may account for its occurrence.

In making a somewhat extended search of the literature of the subject of Meckel's diverticulum and its relations to intestinal strangulation, I can find no record of an exactly similar case. R. H. Fitz in his exhaustive study² does not record a similar instance, but J. W. Elliot³ reports one very much like it, discovered in operating upon a supposed case of acute appendicitis. In this instance, the diverticulum was about seven inches long and of the diameter of the ileum, and had become twisted upon itself at the attachment to the gut and produced strangulation. This case recovered. J. A. Prince⁴ records an instance of a child, aged four years, who had colic for three days, when by abdominal section a diverticulum was found of globular shape, one-quarter inch in diameter at its junction with the intestine, five-eighths of an inch in its greatest diameter, and ending in an elongated cord. Perforation had occurred. T. L. Kelynack⁵ records a largely distended diverticulum, a specimen in the Pathological Museum of the Manchester Royal Infirmary. In 1446 subjects examined by him post-mortem, 18 examples of Meckel's diverticulum were found; this gives a proportion of 1 to 80, or about 1.25 per cent. It was more common in males than in females in the proportion of 11 to 7. The oldest of all these cases was 60, the youngest 13. In no instance was the presence of the diverticulum in any way connected with the cause of the death of the subject. The photograph which he shows in his article was from a patient, aged 42, who died of acute pneumonia. The diverticulum was connected with the ileum by a narrow mouth, $\frac{3}{4}$ of an inch wide, and then extending to a diameter of an inch and rapidly widening into a pouch almost as big as the cæcum. It had a diameter of $3\frac{1}{4}$ inches and a circumference of $10\frac{1}{2}$ inches. It lay quite free in the abdomen and, possibly, its large size may have been due to distension by the intestinal contents. In no instance in all the 18 cases which he records was the lumen of the diverticulum continued to the umbilicus or the abdominal wall. In the Manchester Med. Chronicle

² Am. Jl. Med. Sc., July, 1884, p. 30.

³ Boston M. & S. Jl., June 14, 1894, p. 586.

⁴ Medical News, January 14, 1893, p. 45.

⁵ Brit. Med. Jour., Aug. 21, 1897, p. 459.

(1896, p. 338), he mentions also an instance of a pendulous pear-shaped pouch, discovered after death from sarcoma of the thigh. Thomas Carwardine⁶ reports a case of volvulus of Meckel's diverticulum occurring in a child two days old. The child had been repeatedly sick, bringing up a greenish-brown vomit and had passed nothing per anum, nor was there any discharge from the umbilicus. The distension appeared more on the left side and upon opening the abdomen, there were evidences of lymph upon the surface of the distended intestines from peritonitis and there were numerous adhesions. In making an artificial anus into a mass on the right side of the abdomen, a considerable quantity of meconium escaped. The child died in twenty-four hours, and upon post-mortem examination, it was found that a meconium-containing cyst had been opened, produced by volvulus of Meckel's diverticulum of some three turns. Only a small impervious cord connected it with the bowel below and a minute stalk, which would partially admit a bristle, attached it to the distended bowel above, the junction being a T-shaped one. The special point of interest in this case is the volvulus of the diverticulum occurring in late fetal life in utero. Lionel Beale⁷ describes a case of death due to perforation of a Meckel's diverticulum, fifteen inches from the cæcum. This was nearly three inches long, about the same diameter as the bowel at its origin but increased in size until it terminated in a cul-de-sac, being twice as broad at its lower part as at its origin. It contained a cherry stone and other foreign substances.

Numerous instances of strangulation of the bowel due to the diverticulum being attached to other organs and to the bands formed by the persistence of the omphalo-mesenteric vessels have been reported by D. P. Allen,⁸ A. F. McGill,⁹ C. R. Darnall,¹⁰ and many others, while quite a few instances have been known of an intussusception having its origin in an invaginated Meckel's diverticulum, as in James Adams'¹¹ case and in those mentioned by Treves in his "Intestinal Obstructions," and by others. H. H. A. Beach¹² mentions an instance of pelvic tumor formed by a calcified Meckel's diverticulum uniting the ileum and the bladder.

I have purposely not gone into the anatomical and pathological details of these interesting cases, nor have I attempted to tabulate all those which have been reported, merely mentioning a few of those which have seemed to more nearly resemble my own. Fitz¹³ mentions one case reported by Roth—I have not been able to consult the original reference—in a child a year and a half old, where the pedicle became twisted and hemorrhagic infiltration and necrosis of the mucous membrane occurred with acute peritonitis. He men-

tions also several instances of cyst connected with the intestine which undoubtedly originated as diverticula, and it is to this very elaborate paper I would refer as well as to Doctor Osler's paper in the *Annals of Anatomy and Surgery*, 1881, Vol. IV, and particularly to Frederiek Kammerer's in the *Annals of Surgery*, August, 1897.

The cyst contained two grains of corn, two half peanuts and a fluid, greenish in color and of very foul odor.

DISCUSSION.

DR. KELLY.—Diseases of Meckel's diverticulum, apart from hernia, are certainly rare; in the course of several thousand abdominal sections I have never seen one pathological diverticulum. I am interested in this case particularly on account of the twisted pedicle, the occasion of operation; the torsion of abdominal organs or tumors is a subject still but indifferently understood.

There are undoubtedly a variety of factors which may operate to produce a change of position and hence sometimes of rotation of a body or viscus contained within the abdomen.

I think, further, that the subject of rotation should not be considered alone, but should rather be studied in connection with various other movements, especially those of accommodation or of adaptation of the contained structure to the space in which it is contained, then understanding the various movements which may be impressed upon all bodies we are better prepared in any particular case to explain the cause of the rotation. A lack of employing this wider method of analysis is manifest in the common mistake of trying to explain the rotation of all tumors by one rule often known by the name of an investigator. The following factors must be considered:

1. A growth of the tumor and a consequent change in size and form necessitating change of position.
2. Spontaneous movements on the part of the tumor, as in the case of the lump fetus.
3. Movements impressed upon the tumor by the surrounding hollow viscera or the growing uterus.
4. Movements impressed on the tumor by the contraction and relaxation of the abdominal parietes.
5. Movements resulting from translation or sneeussion of the body, as in walking, lying down and rising, ascending steps, etc.

The position of the body in the abdomen and the character of its pedicle are also factors of the utmost importance.

For example, a long thin pedicle which offers no resistance is best adapted for displacement as well as for the torsion of the body attached to its extremity. A short thick pedicle offers resistance and sessile bodies manifestly cannot be twisted at all.

A body attached somewhere at the periphery is less liable to displacement than one situated more centrally; it is for this reason all the heavier viscera are attached to the walls on all sides, while the intestine designed physiologically to enjoy a wide excursus of movement, is centrally placed with a mesentery which acts like a pedicle.

⁶ Brit. Med. Jour., 1897, December 4, p. 1637.

⁷ Path. Soc. Trans., vol. iii, p. 366, May 4, 1852.

⁸ Med. News, Aug. 13, 1892, p. 177.

⁹ Brit. Med. Jl., January 14, 1888, p. 72.

¹⁰ N. Y. Med. Jl., January 12, 1901, p. 62.

¹¹ Brit. Med. Jour., April 9, 1892, p. 764.

¹² Annals of Surgery, October, 1896, p. 484.

¹³ Am. Jl. Med. Sc., July, 1884.

Examples of rotation are oftenest found in ovarian tumors which do not conform to the physiological type of the viscera either in their location, for they soon grow out among the moving viscera, or in the nature of their attachment, which instead of being sessile is by a more or less attenuated pedicle. There are three important phases in the life history of an ovarian tumor in this connection; in the first place, as it grows it fills the posterior quadrant of the pelvis in which it lies, often pushing the uterus in the opposite direction; next it fills the whole posterior pelvis and projects up through the superior strait; finally, it ends by filling the abdomen more or less completely. While in the pelvis the tumor rarely rotates, as it is splinted on all sides by the pelvic walls, and the largest tumors rarely rotate as they, too, are splinted by the abdominal walls and are too heavy to be impressed by slight forces. I find that the larger cysts are oftener accommodated on the right side under the liver, and I attribute this to the repeated soft impacts of the alternately distending and contracting stomach.

The medium sized ovarian tumors are the ones oftenest twisted, and I consider two factors of great importance in this connection; one is the constant movements of the viscera now collapsed and now distended with food and gases, especially the movements of the stomach; the other is the nipping action of the linea alba on one side of the tumor or the other as it lies in one or other iliac fossa. As the abdominal walls contract the linea is brought nearer to the bodies of the vertebrae and the tumor is caught on one side and the tendency is to turn it.

It is well known that a large percentage of cases of twisted pedicles occur after a confinement; here a most interesting new factor steps in, and that is the sudden translation of the tumor drawn by the collapsed uterus into a new environment. Given an irregular body (tumor) lying within an irregular cavity (abdomen), and granted certain movements, the contained body will seek that position in the container which is

best adapted to its form. It is during this period of readjustment after pregnancy that torsion occurs.

I have spoken in my second rule of spontaneous movements on the part of the tumor (living fetus) deciding its relation to the container (uterus), and this, I think, explains the reason for the position of the fetus in utero.

Dead fetuses offer a large percentage of breech presentations, and this is due to the fact that the relation of the living fetal ovoid to the uterus is not simply that of the actual physical measurement, as in the dead, but is the potential ovoid of the body plus the excursions of the feet. If we enlarge the caudal pole of body by adding the segments of circles described by the feet, we will then have a figure corresponding in form to the interior of the uterus distended with the normal amount of liquor amnii, and the reason of the usual inverted posture is evident.

DR. MITCHELL.—During the last year there has been in Dr. Halsted's service a case which might be of interest in connection with that of Dr. Taylor.

A boy, four years old, was admitted with a strangulated left inguinal hernia. The hernia had been present about a year. The patient was in good condition. On five or six previous occasions there had been difficulty in reduction, and the present strangulation had existed twenty-six hours, being accompanied by great pain, and for the past sixteen hours frequent vomiting. Operation was performed immediately under chloroform anesthesia. In the hernial sac was found a loop of ileum 6 or 8 cm. from the cæcum, and by its side a Meckel's diverticulum, both being constricted at the external ring. The diverticulum was 5 cm. long, 2 cm. in diameter at its base, and 1 cm. in diameter at its tip. The distance of its point of origin from the cæcum was not determined. The cæcum and appendix were presenting just within the external ring. The diverticulum was excised, the bowel dropped back, and the radical operation for the cure of hernia performed. Recovery was uneventful.

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CONGENITAL ABSENCE OF THE ABDOMINAL MUSCLES, WITH DISTENDED AND HYPERTROPHIED URINARY BLADDER.

BY WILLIAM OSLER, M. D.,

Professor of Medicine, Johns Hopkins University.

In the summer of 1897 a case of remarkable distension of the abdomen was admitted to the wards, with greatly distended bladder, and on my return in September, Dr. Fletcher, knowing that I would be interested in it, sent for the child. The accompanying figures, I and II, from photographs, show a very remarkable and unusual pattern of "abdominal tumidity," differing in an interesting way from the picture of the dilated colon in children, and resembling rather that of the ascitic abdomen.

The examination showed that the child had practically no abdominal muscles.

On looking up the literature I can find reports of only two similar cases. In the Clinical Society's Transactions (Vol. 28, 1895), R. W. Parker describes the condition of a newly born infant, weighing five and a half pounds, with a very large, flaccid abdomen, through which the outlines of the intestinal coils could be clearly seen, and the outlines of the abdominal organs easily felt. The abdominal wall was as thin as parchment. Along the middle line, where the rectus muscles should be found, there was little more resistance than over the lateral regions. The oblique and transversalis muscles were apparently quite undeveloped. The umbilicus was not depressed, it was in normal position, but resembled a surface scar. The child died not long after birth. There

was no trace of any muscle representing the transversalis abdominis. There was a thin layer of muscular fibres passing from the cartilages of the ribs to the level of the eighth costal cartilage, where there was the first linea transversa. The body of the muscle was well marked on the right, but on the left it was but faintly seen. Further down there was the merest trace of muscular fibres, representing the rectus on either side. The most remarkable associated condition in this case was the enormous hypertrophy of the bladder, which was situated wholly within the abdominal cavity. There was no obstruction anywhere in the urethra or prepuce. The openings of the ureters into the bladder were quite free. The ureters and pelves of the kidneys were greatly dilated and hypertrophied.

In 1896, Dr. Leonard Guthrie reported to the Pathological Society of London (Transactions, Vol. 47), the history of a male infant, aged nine weeks, pigeon-breasted, very bony and emaciated, with a greatly distended abdomen. Extending between the pubes and the white, linear cicatrix corresponding to the umbilical scar there was a smooth, elastic tumor, corresponding to a distended gall-bladder. The abdominal walls were excessively thin and loose, and seemed to show the coils of the distended intestines on either side, but post-mortem these coils which looked like the intestines

proved to be the enormously dilated and convoluted ureters. The liver, spleen and kidneys could be easily palpated. The child wasted rapidly and died when about ten weeks old. Of the recti only the two upper segments as far as the second linea transversa showed muscular fibres. Below this level no trace of muscle could be discerned. The costal origins of the obliqui and transversales showed muscular structures for about two fingers' breadth below the ribs. The muscles of the back, of the thorax and of the extremities were well developed. Here again the most remarkable features related



FIG. 1.

to the urinary organs. The bladder reached as high as the sear of the navel, and the walls were a quarter of an inch in thickness. The ureters were dilated to the size of the small intestines of an adult, and were remarkably tortuous. After death they exactly resembled, and at first were taken to be, portions of distended small intestine, as they were thought to be when seen through the weakened abdominal walls during life. The orifices of the ureters into the bladder admitted a blow-pipe. There was no obstruction in the ureters; there was no stricture of the urethra, and no phimosis. The kidneys were not enlarged, but the pelves were dilated. The position of the testes was not stated.

An important point in Dr. Guthrie's case was that there

was no trace of a urachus, and the bladder was closely adherent to the inner surface of the umbilical sear, so much so that it could not be removed without the sear and the adjoining portions of the abdominal skin.

The history of my case is as follows:

Claudius K., aged 6, admitted July 13, 1897, complaining of stomach trouble, and difficulty in passing the urine. The chest has been deformed, the mother says, since birth.

The family history is good. One other child; well and strong; parents are healthy.



FIG. 2.

Personal History.—The child was well until the second summer, when he had severe stomach trouble. There have been recurrences of these attacks each year. From the account some of them have been gastric attacks, with nausea and vomiting, but others, and apparently the chief troubles, have been with the urine. The spells last four or five weeks, and they have been getting more frequent. In the intervals he is pretty well and strong, and has a large appetite.

His present attack began about a week ago, and he complained of pains in the abdomen and much burning sensation in passing water. He has become very weak; has not had any vomiting. He has had some headache.

The patient was a poorly nourished child, looking anæmic.

He complained of much pain, chiefly in the hypogastric and lower umbilical regions. On inspection the condition to be described was noted by Dr. Fletcher, but in particular there was a remarkable fulness in the hypogastric and lower umbilical regions, which were occupied by an ovoid mass corresponding to a dilated bladder. The urine which was obtained by catheter was free from albumin, contained a good many leucocytes. The child had a temperature ranging from 99° to 102°. He passed the urine very frequently, an average of from 60 to 70 cc. In the twenty-four hours ending 5.30 on July 13th he passed urine 20 times, a total amount of 1090 cc.; on the 14th he passed urine 18 times, a total amount of 835 cc.; on the 15th he passed urine 15 times, a total of 1060 cc.

The condition was so unusual that on my return in September the case was sent for, and on the 8th I dictated the following note:

In the erect posture the attitude is very remarkable. It is not quite symmetrical, being fuller on the right side than on the left. The navel looks stretched and distended. It is linear, forming a furrow about an inch in length, and below it are furrows in the skin—crow's feet. Above there is seen distinctly on either side the attachment of the recti to the sternum and costal margin. The skin over the abdomen is thin; the veins are a little prominent. When he bends back slight movements of the abdominal muscles beneath the skin are seen.

Recumbent.—Belly flattens out in front, extends at the flanks. Coils of intestines can be seen in peristalsis. Extreme relaxation of abdominal walls; no resistance; fingers can be passed everywhere to the spine. Three fingers can be passed under costal margin over liver nearly 6 cm. The edge of the liver can be felt in its whole extent, and the fingers can be thrust almost as far under it. The bladder could be felt as a firm ovoid body, reaching almost to the navel.

Spleen can be felt on deep pressure. Both kidneys can be felt.

He cannot raise himself off the bed without turning over. As he makes the attempt the abdomen is thrust forward and slight contraction is seen of the expanded abdominal muscles and recti.

The deformity of the thorax is very remarkable. Harrison's grooves are unusually marked, corresponding to the 6th costal cartilage. The lower portion of sternum is thrust forward, forming almost a right angle with the xiphoid cartilage. As shown in the photograph it is remarkably prominent, and is fully 3 cm. above the level of the skin in the intercostal furrows.

There is a condition of cryptorchidismus. The testes are not to be felt in the groins.

Remarks.—These cases illustrate a very remarkable form of congenital defect. The deficiency in the abdominal muscles, and the high position of the bladder are associated conditions due to arrest of development. We could not say definitely in my case whether the bladder was adherent to the umbilical scar. Dr. Guthrie regarded the hypertrophy of the bladder and the dilatation of the ureters as secondary, due to the fact that in his case, being firmly connected with the umbilical scar, it was unable to contract downward and to empty itself completely. In its effort to do so it became hypertrophied and dilated, and the accumulation of urine caused backward pressure and dilatation of ureters.

In reply to a question, Dr. Bardeen, one of Prof. Mall's associates in the Anatomical Laboratory of the Johns Hopkins University, who has been specially engaged in a study upon the development of the muscles, writes as follows: "Two possibilities suggest themselves to me in the case:

"1. It is possible that the lack of resistance normally met with in the abdominal wall by the bladder at the time the kidneys begin to secrete urine may cause the bladder to expand rather than to empty secretions into the amniotic cavity through the urethra.

"2. Under normal conditions the growth of the abdominal musculature into the *membrana reunions*, the early covering of the abdominal cavity, is preceded by the formation of a vascular plexus supplied from above by the internal mammary, from below by the epigastric artery. It is possible that an abnormal arrangement of the blood vessels in the embryo prevented the formation of this plexus, and impeded the growth of the abdominal musculature, and that at the same time circulating disturbances gave rise to the abnormal conditions found in the bladder and ureters."

ON A FAMILY FORM OF RECURRING EPISTAXIS, ASSOCIATED WITH MULTIPLE TELANGIECTASES OF THE SKIN AND MUCOUS MEMBRANES.

BY WILLIAM OSLER, M. D.,
Professor of Medicine, Johns Hopkins University.

The association here described is rare, as, after a careful search through the literature, I can find but one reference to a similar case.

An hereditary form of epistaxis has been well described by Babington.¹

The association of epistaxis with angiomas of the nasal septum has long been known; but for the associated condition of multiple telangiectases of other mucous membranes and of the skin, I have been able to find only the following report by Rendu.² A man, aged 52, whose father had had

¹ Lancet, 1865, ii, p. 362.

² Gaz. des Hôpitaux, 1896, p. 1322.

repeated attacks of melena, and whose mother and brother had been subject to epistaxis, was admitted in a condition of profound anæmia, having had for three weeks a daily recurrence of epistaxis. He had had his first attacks of bleeding from the nose at the age of twelve, and had been subject to them ever since, particularly in the spring. He had never had any other hæmorrhages. On the skin of the nose, of the cheeks and of the upper lip there were numerous small red spots due to dilatation of superficial vessels of the skin. Similar small telangiectases were seen on the internal surfaces of the lips, the cheeks, the tongue, and on the soft palate. The punctiform angiomas were not seen on the mucous membrane of the nose.

In the three cases here described, two belonged to a family in which epistaxis had occurred in seven members. Both of my patients had had bleeding at the nose from childhood, and both presented numerous punctiform angiomata on the skin of the face and of the mucous membrane of the nose, lips, cheeks and tongue.

The third patient had suffered in an unusual degree from recurring epistaxis, and the telangiectases were most abundant over the body, and very numerous also on the mucous membranes.

The condition has nothing to do with hæmophilia, with which the cases had been confounded.

CASE I.—Attacks of Epistaxis from boyhood; seven members of the family subject to it. Telangiectases on skin of face and on mucous membranes of nose and mouth.

George B., aged 57, a seaman by occupation, admitted to the Johns Hopkins Hospital May 31, 1897, with anæmia and swelling of the feet.

Family History.—The father died at 69, of stone in the bladder. From boyhood at intervals he had had bleeding from the nose, never, so far as his son knows, from any other situation, nor does his son think that he bled specially from cuts. The bleeding was very frequent, generally, the son says, every day. So far as he remembers he never was in any danger from it.

The mother, who is living and well, aged 81, has never had epistaxis. He does not know of any members of his father's or mother's families who were bleeders.

Brothers.—Two died suddenly, one aged 47, the other aged 57. Neither had ever bled from the nose. He does not know the cause of death. The history of a third brother, who has had epistaxis from boyhood, will be given subsequently.

Sisters.—One died at 59, of Bright's disease. She was a large, stout woman, and had been subject to epistaxis from childhood. A second sister, the mother of fourteen children, died several years ago in childbirth. He does not know whether it was from hæmorrhage. She had bled from childhood both from the mouth and nose. He does not know whether she had any "spots" on her nose or lips.

In the third generation, this patient has one child, aged 13, who has bled occasionally from the nose. He has never

heard that any of his nephews or nieces have bled, but a grandniece, granddaughter of the patient's elder sister, has had epistaxis frequently.

Personal history.—He had been a sailor for forty-three years. He had been a moderate drinker. He had had syphilis thirty years ago. With reference to the epistaxis, he does not remember to have had it before his tenth year. The attacks were not very severe, but recurred almost every day. He was able to go to school, and later to his work. Twenty years ago, when he was thirty-seven, the condition became much more serious, and for nearly three years he was unable to do any work on account of the weakness and anæmia induced by the bleeding. He seems to have had a great deal of prostration, and says that for nearly five months he could not use his left arm. He has never bled from cuts, and never from the gums. While in the Navy, in 1862, he bled profusely from one of the angiomata on the lower lip, also from a very small one on the skin of the septum. He has frequently been very anæmic, and has had swelling of the feet and shortness of breath. He has had hæmorrhoids for thirty years, and fourteen months ago had them removed at the Marine Hospital. He has bled indifferently from right or left nostril. Latterly the bleeding has become much more aggravated, and he has become very anæmic.

Present condition.—The patient was a large framed, well nourished man, very intelligent. He was short of breath, the face looked a little swollen, suffused and anæmic; the feet and legs were swollen. The blood examination gave 2,980,000 red blood corpuscles, leucocytes 8000, hæmoglobin between 15 and 20 per cent. The nostrils were very capacious, and there was a clot of blood projecting from the left orifice. He had bled up to time of admission. The coagulation time as taken by Wright's tubes ranged from five and a half to seven minutes.

The general surface of the skin was pale, a little yellow. No hæmorrhages were seen except on the right elbow where was a rounded area of subcutaneous extravasation about 1½ cm. in diameter. The face presented a very unusual appearance, owing to the large number of dilated venules and capillary and venous telangiectases. They were most abundant on the ears, the skin of which presented a remarkable appearance, partly from the dilatation of the venules, which could readily be seen, and partly from the bright red capillary telangiectases. There were some dilated venules on the nose and cheeks, and the lips present a number of angiomata, particularly on the mucous surface, and just at the junction of it with the skin. There were one or two small ones about the skin of the nostrils, and subsequent examination showed numerous angiomata on the mucosa of the septum, particularly on the cartilaginous portion.

The mucous membrane of the mouth looked normal, but the tongue, on the tip and along the edge for a little distance, showed a number of telangiectases.

There was no albumin in the urine; the specific gravity was 1010, no casts. His legs were swollen to the middle of the calves. There were dilated venules on the outer aspect

of the legs. The edge of the spleen could just be felt. The liver was not enlarged. The apex beat of the heart was felt just under the right nipple. There was a soft systolic murmur at the apex, and a louder one along the left sternal border. The bleeding stopped shortly after admission.

On May 25, he had a slight attack of epistaxis, which lasted for thirty minutes. The general condition had much improved. The œdema had disappeared from the extremities, and he had gained rapidly. The blood condition improved, and on the 25th the red corpuscles were 3,224,000.

This patient has reported at intervals at the Dispensary through 1898, 1899 and 1900. He has had bleeding from the nose at intervals, lasting for a few hours at a time. When last seen he looked very well, though a little anæmic. There has been no special change in the cutaneous telangiectases.

CASE II.—*Epistaxis from childhood; Telangiectases of skin and mucous membranes, bleeding from some of the spots. Cancer of the stomach, death, autopsy.*

William B., aged 55, admitted Jan. 20, 1899, complaining of stomach trouble.

Family History given with Case I.

Personal History.—He began to bleed from the nose very early in life; he does not remember exactly the date. It has been a source of constant trouble, and has on several occasions caused extreme anæmia and weakness. He usually bleeds without any provocation. He has never bled freely from cuts, but on several occasions spots on the face have bled after shaving, and he has bled from the red spots on the lips. Of late years he has bled less frequently than when he was a younger man. He has been a sailor, and has led a very irregular life; has used tobacco freely, and has been at times a very heavy drinker.

He came into the hospital complaining of nausea, vomiting and pain in the abdomen, which he had had for some months.

Present Condition.—The patient looked pale and sallow, and there were numerous small varicose veins on the skin and mucous membrane of the lips, and on the side of the nose, a few on the cheeks and on the ears. On the tongue there were a number of small red spots, evidently of the same nature. The same spider-like angiomas could be seen on the mucous membrane of the septum of the nose. They were not so numerous nor so striking a feature as in his brother's case, though those upon the mucous membrane of the lips were large enough to at once attract attention. The patient had a large tumor mass in the abdomen, evidently a new growth of the stomach.

Blood examination the day after admission: r. b. c. 4,488,000; leucocytes 7400; hæmoglobin 71 per cent. The blood coagulation time on Jan. 20th was eleven minutes; on the 22d, it was eleven minutes; on the 25th it was eleven minutes; on the 26th it was nine and a half minutes. He had repeated bleedings, and then on January 31st the coagulation time

was four minutes. After he had been taking calcium chloride, fifteen grains three times a day for three days.

He bled freely from the nose two days after entering the hospital, and was given 250 cc. of a one per cent gelatin solution hypodermically. The blood coagulation time was reduced to one and a half minutes.

On January 30th he had two bleedings from the nose, and again on the 31st. On Feb. 6th he vomited coffee-ground material. On Feb. 9th he had another bleeding from the nose. On Feb. 10th the blood coagulation time was one minute. On Feb. 18th he had a right hemiplegia. He grew progressively weaker, and died on Feb. 24th.

The anatomical diagnosis was: cancer of the stomach, mesentery, omentum, liver, retroperitoneal glands, lungs and brain. Angiomas in mucous membrane of the nose and of the stomach. In the stomach there were a dozen round foci, each 3 to 4 mm. in size, which at first looked like ecchymoses but were dilated venules and capillaries.

Sections of the septum of the nose made for me by Dr. Austin, showed many large dilated veins just beneath the epithelium.

CASE III.—*Recurring Epistaxis from the 10th year—Multiple Telangiectases of skin and mucous membranes of nose and mouth.*

M. W. C., Inez, Martin Co., Ky., aged 49, was admitted to the Johns Hopkins Hospital, August 28, 1896, complaining of epistaxis, which had recurred at short intervals from his boyhood.

His mother died of consumption; she had had inflammatory rheumatism. His father died of Bright's disease. He has three brothers and one sister living; one sister died of consumption. So far as he knows there are no 'bleeders' in his family, and none of the members have had serious attacks of epistaxis.

With the exception of epistaxis, the patient has been a healthy man. He had typhoid fever when twenty years of age. He has never had rheumatism. He had gonorrhœa at eighteen. He has never had syphilis. He has used alcohol in moderation. He was a very active boy and took a great deal of exercise. When ten years old he began to have epistaxis, which often followed the trick of walking upon his hands. He would bleed quite profusely for part of a day, or for some hours every day or two for ten days or more, until he got quite weak and anæmic. The attacks were sometimes of much greater severity than at others. For some years he did not pass a week without bleeding from the nose. It usually began as an oozing, and then would end in a very free hæmorrhage, lasting from a few minutes to half an hour. Between his eighteenth and twenty-fifth years he was very much better, and it was thought that perhaps the tendency had been checked. It did not stop entirely, but he was very much better. Then it recurred, and during all these years he does not think he has passed a week without some bleeding from the nostrils, from either one indifferently.

He has been an active business man, and the bleeding has interfered very much with his work, as he would get pale and very weak. He has often had to have the nostrils plugged, and at times after severe bleeding he would get very pale, and as he said, "the blood would be so watery that my feet would swell." He never has had any hæmorrhages into the skin, but he has had at intervals bleeding from the 'spots' on the gums and lips, he thinks perhaps as often as twenty-five times. When a lad (he cannot fix the exact date), he noticed reddish spots on his face and about his hands; they have persisted and have increased in number during the past seven or eight years. He has never had any other hæmorrhages than those mentioned.

Present condition.—The patient was a very well nourished, robust looking man, pale (as he had recently had a very severe hæmorrhage), with all the outward evidences of anæmia. The blood count was: red corpuscles, 3,460,000; hæmogoblin 38 per cent. There was marked poikilocytosis; the leucocytes were normal in number. The differential count gave lymphocytes 10 per cent, large transitional forms 9 per cent, polymuclear 80 per cent, eosinophiles 1 per cent. The lymphatic glands were not enlarged. There were hæmie murmurs at the base of the heart, and a soft systolic at the apex. Neither spleen nor liver was enlarged. The coagulation time, as taken by Wright's tubes, was two minutes and a half.

The telangiectases.—These were most numerous on the face, which was much disfigured by them. On the right cheek there were twenty-five, some of which projected slightly beyond the skin as purplish spots from 1 to 4 mm. in diameter; the largest presented a stellate arrangement of veins. On the left cheek there were about twenty, several with quite large veins passing to the centre. While most of them were quite superficial, there were others subcutaneous and bluish in tint. On the lower lip the edge at the skin was closely set with them, and on the mucous membrane of the left side there was an angioma the size of a split pea. On the upper lip there were many small ones, and in the very centre, just at the raphé, there was a large, deeply seated, blue one. Scattered over the forehead were eight or ten, most of them purplish red, one or two near the margin of the scalp deep seated and blue. Here and there on the scalp a few could be seen. On the upper surface of the tongue there were five or six, and several on the under surface, all of them small and very bright red in color. There were none on the pharynx, but there were a number on the inner surfaces of the cheeks and on the gums, which were not swollen. The skin of the ears presented numerous pin point telangiectases, giving to it a very peculiar appearance; the spots were about the size of the central point of a flea bite.

Scattered over the back, chest and abdomen were two or three dozen bright red angiomas, none of them more than 2 or 3 mm. in diameter. Several of them project, and one or two are almost pedunculated. The arms and legs are practically free. On the hands, however, there are a good

many angiomas, nearly all small and pin point. They are scattered over the fingers and palms, particularly about the pads of the fingers.

Dr. Warfield made several careful examinations of the nose, and reported that on both sides of the septum there were numerous scattered angiomas, very similar in appearance to the smaller ones on the cheeks, and tortuous veins could be seen radiating from their centres. With the exception of these spots the mucous membrane of the nose and throat looked normal.

The patient remained in hospital until September 18th. In the first ten days there were six bleedings from the nose. On September 9th Dr. Warfield thoroughly cauterized the angiomas on the septum. The operation was followed by quite profuse hæmorrhage, which was readily stopped. On the 10th the hæmorrhage recurred and he lost 580 cc. of blood before it was checked by plugging. Half an hour later he had a second hæmorrhage in which 820 cc. were lost. Within twenty-four hours he bled 1400 cc. He was not very much prostrated, but looked a little pale. This was the largest bleeding he had had while in the hospital, but he said he had not infrequently had much more profuse hæmorrhage. Between the 10th and the 18th, the day of his discharge, he had no bleeding.

Subsequent history.—Patient heard from June 5th, 1897. He stated that he had been better than for any time for the past ten years, but he still has occasional bleeding for a day or two pretty freely. He thinks that the cauterization has saved his life. He has been so much better since it was done. After bleeding for a few days he takes the iron and arsenic.

Oct. 11, 1897, I had a note from this patient to the effect that he had had very severe bleedings during the past three weeks.

Jan. 5, 1898. He has been bleeding very badly for the past five weeks, and is in a very weak, critical condition.

Dec. 16, 1898, he writes, "I am still troubled with the hæmorrhages, but am able to attend business. I have procured in the last three months a gum arrangement, which I insert and inflate with air, and keep it in for fifteen or twenty-five minutes, and it stops the bleeding entirely. It is a great improvement on the old plan of plugging with cotton or anything else. I can use it at once myself, and it causes no pain. Since I have had it I am holding my blood, and I think now I will get stronger."

He sent a diagram of a very ingenious arrangement. He took a rubber finger-stall about three inches long, into which was tied a small bit of rubber-tubing, with a stop-cock at one end. He inserted the finger-stall, relaxed, then put the tubing in his mouth, inflated it, and turned the stop-cock.

Nov. 16, 1899. Patient heard from to-day. He says that with the instrument above described he has succeeded in "holding his blood." Still bleeds a little, but not so frequently as he used to do. He has been able to attend to business.

REMARKS.

Angiomata are very peculiar and remarkable structures, in which I have been interested for many years. Apart from the big nevi and angiomata with surgical relations there are:

1. The pin-point, punctiform, capillary angioma, of which few skins lack examples. They may be numerous, but they are rarely disfiguring. They appear and disappear. For ten years I had one the size of a pin's head on a finger.

2. The solid, nodular nevus, ranging from 1 to 4 or 5 mm. in diameter, forming a definite little tumor, either sessile or pedunculated, and very common on the back.

3. The spider angioma, formed by (a) three or four dilated veins, which converge to and join a central vessel; or (b) which unite at a central bright red nodule projecting a little beyond the skin. They are very common, and doctors are often consulted about their presence on the face.

As examples may be found on the skin of nearly everybody, these three varieties may be regarded as almost normal structures.

When the punctiform or spider angiomata increase greatly in numbers they are very disfiguring. In Case III the skin of the face was peppered with them, and at a distance the patient looked disfigured with a bright, fresh acne rash. In Case I they had also proved a source of danger, as he had

bled from them repeatedly. An individual spider angioma may increase in size, or, as in the cases I have here related, they may become very numerous.

Angiomata have a curious relationship with affections of the liver. In cirrhosis, in cancer, in chronic jaundice from gallstones spider angiomata may appear on the face and other parts. They may be of the ordinary stellate variety, like the stars of Verheyen on the surface of the kidney, or the entire area of the star may become diffusely vascularized, so that there is a circular or ovoid territory of skin looking pink or purple, owing to the small dilated venules. A dozen or more of these may appear on the trunk, or even large ones may disappear. And lastly, in a few cases of disease of the liver I have seen large, mat-like telangiectases or angioma involving an inch or two of skin, and looking like a very light birth-mark, but which had appeared during the illness. The skin was not uniformly occupied with the blood vessels, but they were abundant enough on the deeper layers apparently to give a deep change in color and to form very striking objects. The dilated venules on the nose, and the chaplet of dilated veins along the attachment of the diaphragm are not infrequently accompaniments of the spider angiomata in cases of disease of the liver.

I have recently seen the spider angiomata appear in the face in a case of catarrhal jaundice.

ON THE BEHAVIOR OF EPINEPHRIN TO FEHLING'S SOLUTION AND OTHER CHARACTERISTICS OF THIS SUBSTANCE.

BY JOHN J. ABEL, M. D.,

Professor of Pharmacology, Johns Hopkins University

It is a well established fact that epinephrin, the blood pressure raising constituent of the suprarenal gland, is an energetic reducing agent for such salts as silver nitrate, the chlorides of gold and platinum, and potassium ferrocyanide, but it has been proved entirely unable to reduce Fehling's solution even on boiling. In my first paper¹ on the active principle of the suprarenal gland, especial attention was given to this point. Tests with impure extracts of the gland were not alone relied on, a benzoyl compound of epinephrin was saponified by boiling its solution in glacial acetic acid with an equal volume of 25% sulphuric acid, and with the products of this saponification all tests were made. The results were negative, Fehling's solution was not reduced. v. Fürth² later, also prepared and saponified this benzoyl compound as well as an acetyl derivative of his own, and he seems to have found nothing to conflict with his former views, that the native principle does not reduce Fehling's solution.

Fraenkel,³ Moore,⁴ Metzger,⁵ and v. Fürth⁶ have also shown that more or less purified extracts of the gland do not reduce Fehling's solution, and I have failed to obtain this reduction by the use of similar extracts, made in my earlier experiments from sheeps', and in my later, from beeves' suprarenals.

The method employed by me in the preparation of these extracts precludes the occurrence of either reduction or oxidation, except in so far as the latter might be induced by exposure to air. The glands were digested in some instances with pepsin, in others with papoid ferment, and only methods of solution and precipitation with organic fluids, such as alcohol, acetone, toluol and ether were employed.

In the case of these extracts, the failure to reduce Fehling's solution might possibly be attributed to some disturbing

¹ Abel and Crawford, this BULLETIN, July, 1897.

² Zeitschr. f. Physiol. Chem. Bd. xxvi, S. 15.

³ Wiener med. Blätter, 1896, No. 26, p. 409.

⁴ Journ. of Physiol., vol. 17, Proc. Physiol. Soc., p. xiv.

⁵ Zur Kenntniss der wirksamen Substanzen der Nebennieren. Diss. Würzburg, 1897.

⁶ Zeitschr. f. Physiol. Chem., Bd. xxiv, S. 142.

substance which interferes with the reaction. In the case of the benzoyl compound, it might be charged that the active principle was oxidized, either in the process of benzoating or in the subsequent saponification, and that it was, perhaps, originally able to reduce Fehling's solution. This appears less probable when it is remembered that the active principle is still able to reduce silver nitrate and other salts after its liberation from its benzoyl compound by the method just cited.

The iron compound of v. Fürth also does not reduce Fehling's solution. Here again it might be asserted that the power to do so was lost by oxidation in the preparation of this iron salt, but this assumption, like the above, is without experimental foundation, for the reason that the properties of the substance as contained in this iron compound, remain unchanged in all other respects. The possibility of an oxidation in the preparation of this compound is not denied. There is, however, no reason to assume that its occurrence would abolish the power to reduce copper sulphate and not affect its behavior towards other salts.

Lastly, as will presently be shown, an apparently pure sulphate or bisulphate obtained from a basic lead precipitate of aqueous extracts which have been made by extraction of the glands with very dilute sulphuric acid and zinc dust, also fails to reduce Fehling's solution on boiling. There appears to be no ground for the assumption that oxidation took place in the course of the precipitation with basic lead acetate.

Existing evidence, therefore, points to the conclusion that epinephrin in its active, unaltered state is not capable of reducing Fehling's solution.

It will now be demonstrated that this additional property can easily be conferred upon this substance without changing its behavior to other metallic compounds. It is then, however, modified in several of its physical characteristics. Its solutions, for example, are not quite so rapidly oxidized on exposure to the air, and the free reduced base, as prepared by Takamine and Aldrich, is non-hygroscopic and capable of crystallization. This point, therefore, is of importance in the elaboration of methods for isolating this principle. The salts of this modified form of our substance are, however, as hygroscopic and difficult to crystallize, as are those of the unaltered substance.

This change of native epinephrin to the copper sulphate reducing form, is best effected by means of sulphuretted hydrogen, as illustrated in the following experiment.

After decomposition of v. Fürth's lead precipitate of impure epinephrin (suprarenin) in the manner described by that author, and after repeated solution in methyl alcohol of the sulphates thus obtained, and repeated fractional precipitation with ether, there is finally obtained a hygroscopic, amorphous sulphate or bisulphate of native or unaltered epinephrin which possesses a high degree of purity. This salt is amorphous when finally washed with ether and dried, but in the final precipitations with ether, it is thrown out of its methyl alcohol solution in what appears to be a

minutely crystalline condition. The little particles that settle on the sides of the flask look like crystals when viewed through the ethereal fluid with a pocket lens. However, in the subsequent washings with ether the salt absorbs water on account of its hygroscopic qualities, and in consequence the crystals take on an amorphous character.

This method yields a salt of at least as high a degree of purity as adrenalin, as is proved by its physiological activity and by colorimetric comparisons with adrenalin, in which the latter is dissolved in an amount of sulphuric acid estimated to be equivalent to that contained in the sulphate. In these comparisons the fine green tint developed by dilute ferric chloride was employed as a means of comparison and no difference could be detected between the two. The proof of its high physiological activity was furnished in the experiments made with it by Prof. Reid Hunt, and published by him in the American Journal of Physiology for March, 1901. No investigator has thus far worked with a more active specimen of the blood pressure raising constituent, as will be seen by a comparison of Hunt's data with any others published. It will, I think, be admitted that this salt was sufficiently pure to furnish conclusive evidence that unaltered epinephrin cannot reduce Fehling's solution.

By the following method its character in this regard can be entirely changed. If hydrogen sulphide be passed through an aqueous solution of the salt it soon becomes turbid in consequence of the liberation of sulphur. In case the solution has been thoroughly charged with the gas, if it is cooled and set aside for a few hours, the deposition of sulphur appears to increase. If then filtered, repeatedly shaken with chloroform and concentrated in vacuo until all traces of hydrogen sulphide and chloroform have disappeared, it promptly reduces Fehling's solution on boiling. All methods of isolation, therefore, that involve the use of hydrogen sulphide or of alkali sulphides will yield a modified or reduced form of the active principle, provided, in the case of hydrogen sulphide, the gas is passed into a solution whose reaction is only slightly acid. The adrenalin of Takamine is such a reduced form, as it is also easily oxidized by Fehling's solution, a fact which seems to have escaped the notice of Takamine and also of Aldrich, who has lately prepared adrenalin by a method which involves the use of hydrogen sulphide.

Other methods of reduction also effect the change just described. Thus: a purified extract of the gland, which consists largely of native epinephrin is dissolved in alcohol containing hydrochloric acid, and is then reduced by boiling with granulated tin and strips of platinum for six hours or more. After cooling, the solution is filtered and the filtrate precipitated with alcoholic solution of ammonia. In this way a small yield of a tin compound of reduced epinephrin is obtained. On being washed and dried, the compound presents the appearance of a white powder, not very soluble in water but intensely active in a physiological way. It reduces Fehling's solution on boiling for a minute or two. If the compound be boiled in water with zinc dust, thus replac-

ing the tin with zinc, the resulting compound also reduces Fehling's solution.

If the tin is removed by means of hydrogen sulphide in the presence of a dilute acid a hygroscopic salt may be prepared which also reduces alkaline copper salts.

This unstable substance is also capable of self-reduction. It has just been stated that when its benzoyl compound is saponified in a mixture of glacial acetic and 25% sulphuric acid, the change into the copper sulphate reducing modification does not occur.

When, however, either the benzoyl or acetyl compound is saponified in the autoclave, with water alone or with a 1% solution of sulphuric acid, and under a pressure of two or three atmospheres, this alteration is brought about. That this fact was not mentioned in my earlier papers is accounted for by a neglect to apply Fehling's test when the methods of saponification were changed. My earlier work, and also that of others, had shown that when epinephrin is boiled with mineral acids in open vessels or in sealed tubes, no reducing substance is obtained, and it was only later, after I had found how the substance is altered by hydrogen sulphide, that I again applied the test to my series of autoclave products.

The reduced product, as obtained by the use of the autoclave differs, however, in a few particulars from that obtained by the use of hydrogen sulphide and other chemicals. The former product appears to be even more easily oxidized; it is certainly more sensitive to the action of alkalies and to exposure to the air. Furthermore, the addition of very dilute ammonia nearly to the point of neutralization causes the reduced product from the autoclave to fall out of even a dilute solution in the form of white flocks, which rapidly assume a reddish brown and finally a dark brown color. When this flocculent precipitate is washed with alcohol and ether, and dried, it is found to have lost its physiological activity. It is also precipitated by a number of alkaloidal reagents, a point to which I have called attention in a previous paper.⁷ From some of these differences it might be concluded that the autoclave product is further reduced than that treated with hydrogen sulphide. Analyses and quantitative tests with alkaline copper solutions must settle this point. When a dilute solution of the reduced commercial compound called adrenalin, which fails to give a precipitate with ammonia, is slightly acidulated with sulphuric acid, and then treated in the autoclave under a low pressure as in the saponification experiments above described, no black resin or oxidation product is thrown out, but the solution, while retaining its reducing power for alkaline copper salts has developed the additional characteristics just alluded to.

A suggestion as to the action of hydrogen sulphide and of reducing salts and also in respect to the similar effect produced in the autoclave, is now in order.

It would be strictly in agreement with chemical experience

if we were to assume that the agents named cause this unstable substance, which already possesses the power to reduce many metallic compounds, to take up more hydrogen.

The analogous change produced in the autoclave, must evidently be classed with other examples of self-reduction. I have elsewhere stated that a considerable loss of material occurs when this apparatus is employed, as a large part of the epinephrin is deposited in the form of an insoluble and resinous oxidation product. It is apparent, then, that oxidation and reduction go on simultaneously in the autoclave.

Whether the mechanism of the reduction is alike in all the instances cited above, and whether it consists in the assumption of hydrogen or in the loss of oxygen, must finally be decided by analysis.

ON THE RETENTION OF A BENZOYL RADICLE IN MY FORMER SERIES OF EPINEPHRIN COMPOUNDS.

Attention may now be called to another point in which the autoclave is concerned. I have repeatedly stated that my whole series of epinephrin compounds was derived from an original benzoyl compound, the form in which epinephrin was isolated from the gland, and that this compound, which is entirely insoluble in water, was saponified in the autoclave. My analyses forced me to assign the formula $C_{17}H_{15}NO_4$ to the active principle, both in its physiologically active and in its inactive modifications.

Later work has shown me that my whole series of derivatives contains an unsaponified benzoyl radicle. That this benzoyl group escaped the fate of its fellows could not be known with certainty until epinephrin should be isolated by other methods. I early became aware of the fact that when the epinephrin bisulphate of my early papers is subjected to destructive treatment, such as heating in a sealed tube at $150^{\circ}C$, with 25% hydrochloric acid, an ether-soluble acid, which in every way resembles benzoic acid, is split off from it. I stated this to be the case in a paper published in the *Zeitschrift für Physiologische Chemie*, Vol. XXVIII, p. 348, and I will here add that the melting point of this acid, after only once subliming it from the ether residue was $120^{\circ}C$.

In repeating this work I have found that it is only necessary to treat inactive epinephrin, the highly active bisulphate of my former papers, in a test tube with nearly concentrated sulphuric acid, heating gently over a free flame, then diluting with water and extracting with ether, to secure benzoic acid in abundance. The iron compound of v. Fürth, which is a derivative of native epinephrin, as also the reduced compound called adrenalin, yield nothing whatever when treated in the manner described. Instead of finding the bowl from which the ether is evaporated lined with crystallized benzoic acid, one finds in the case of these compounds merely a trace of an amorphous fatty substance. I have not thought it necessary to make a quantitative estimation of the benzoic acid that is thus split off from epinephrin, since a preliminary analysis of adrenalin and also of the acetyl derivative of v.

⁷ This BULLETIN, March, 1901.

Fürth's ferri-suprarenin had shown me that a single benzoyl radicle accounts fully for the quantitative differences in the composition of these several modifications of what is one and the same substance.

In order to arrive at the true formula for reduced epinephrin we must therefore subtract from $C_{17}H_{15}NO_4$ the retained benzoyl group (C_6H_5CO), and restore the hydrogen atom that was displaced by the radicle. This will give us $C_{10}H_{11}NO_3$ as the empirical formula for reduced epinephrin. In accordance with this change in terminology, $C_{17}H_{15}NO_4$, the form in which this principle was first isolated by me, and which yields stable and non-hygroscopic salts, should now be called mono-benzoyl reduced epinephrin. The term reduced, as already stated, applies to the product as altered by hydrogen sulphide and other reducing agents. The native substance, very soluble, apparently very hygroscopic, less stable and non-copper-reducing should be called native or unreduced epinephrin. This variety of the substance has been isolated by me as the hygroscopic sulphate or bisulphate which was employed in the experiments with hydrogen sulphide previously described.

COMPARISON OF EPINEPHRIN WITH THE SUBSTANCES KNOWN AS SUPRARENNIN AND ADRENALIN.

Contemporaneously with my paper published in this Bulletin for Sept.-Oct., 1898, in which I showed that the blood-pressure-raising substance as isolated by my methods is represented by the empirical formula $C_{17}H_{15}NO_4$ and in which I had proposed the name epinephrin for this substance, appeared a paper by O. v. Fürth,⁸ who declared the substance in question to be either tetrahydrodioxypyridin, $C_5H_9NO_2$, or dihydrodioxypyridin, $C_5H_7NO_2$. In a later paper⁹ containing no further analytical data, the author describes the isolation and preparation of a new iron compound and proposes the name suprarenin for our substance. In it he makes the erroneous statement that epinephrin is something entirely different from the true blood-pressure-raising principle and that its resemblances to this principle are due solely to a slight contamination with it, a mistake into which he was evidently led by a very imperfect and faulty repetition of some of my work, the neglect to consider that this highly sensitive and unstable substance develops new characteristics with each change of method, and also by the very important omission to analyze either his iron compound or its derivatives.

I need only point to a recent paper¹⁰ in reply to v. Fürth, to the analysis of the acetyl derivative of his iron compound which will presently be given and to Aldrich's analysis of the adrenalin of Takamine to show how entirely without foundation is v. Fürth's assertion that either $C_5H_9NO_2$ or $C_5H_7NO_2$ represents the composition of epinephrin, or, of

what he calls suprarenin. This inadequate formula was derived by him from the analysis of an acetyl derivative which was made directly from a highly impure extract containing other substances equally capable of being acetylated and it was not fortified by analyses of derivatives.

From all that has been said here and in an earlier paper it will be seen that suprarenin is nothing else than epinephrin, that is, it is equivalent to a non-reduced form of this substance, freed from the included benzoyl group.

It is possible that in the formation of v. Fürth's ferri-suprarenin, the only derivative even approximately pure that he has thus far prepared, an oxidation of the native principle occurs. On this assumption his suprarenin would not represent the native or non-reduced form of the substance, but rather an oxycompound. As pointing to this conclusion the following experiment may here be cited. More than a year ago, I prepared an acetyl derivative from ferri-suprarenin. Since it is difficult to purify this iron compound, its acetyl derivative was saponified in the autoclave, the liberated suprarenin was transferred into a picrate by extraction with acetic ether after the previous addition of a solution of picric acid, and the picrate thus obtained was transferred into a sulphate by the methods described in previous papers. This sulphate was now acetylated and the resulting amorphous, dark colored compound dried over sulphuric acid in vacuo and analysed. The following percentages of carbon, hydrogen and nitrogen were obtained:

Found.	Required for $C_{10}H_{11}NO_4(CH_3CO)_3$
C = 57.51	C = 57.31
H = 5.05	H = 5.07
N = 4.27	N = 4.18
N = 4.18	

The two nitrogen analyses were made by the method of Kjeldahl. A duplicate analysis for carbon and hydrogen made from a specimen dried at 110° gave somewhat higher percentages than the above, and is not here given, as decomposition had undoubtedly taken place. The assumption that this product contains three and not four acetyl groups, is in line with v. Fürth's contention that the native substance takes up three acid radicles.

On this assumption, the above analysis would lead to the rational formula $C_{10}H_{11}NO_4$, instead of $C_{10}H_{11}NO_3$. The additional atom of oxygen may have been taken up either in the course of the formation of the original iron compound, or in the process of acetylating it. Although unable to decide this point, I have presented the above analytical data to show how exact an approximation to my formula may be obtained in the case of a derivative which is made from so called suprarenin.

It is freely admitted that my empirical formula may, in the future, when a more perfect series of compounds shall have been made, prove slightly incorrect. Even then the fact will remain that the isolation of epinephrin was first effected by my methods, admittedly capable of improvement as these are.

⁸ Zeitschr. f. Physiol. Chem. Bd. xxvi, S. 15.

⁹ Ibid. Bd. xxix, S. 105.

¹⁰ This BULLETIN, March, 1901.

The more recent work of Takamine and of Aldrich may now be considered.

The former¹¹ has the credit of having devised a method by which the free reduced and physiologically active base may be manufactured on a commercial scale and this modification of epinephrin has been named adrenalin. Its reducing power for copper sulphate, its relatively greater stability, its very slight solubility in water and its non-hygroscopic and crystalline condition are among the characteristics that distinguish it from the native principle as it exists in the gland. Crystalline salts, which are non-hygroscopic and maintain their form on exposure to air have not yet been made from it.

Adrenalin agrees with my earlier compounds, notably with the picrate and bisulphate, in all of the properties alluded to, with the exception of its more ready and permanent crystallization. In an earlier paper statements will be found regarding the extent to which some of my salts were crystalline, and I may here add that in the course of preparation of a picrate of my phenyl di-carbamic ester of mono-benzoyl reduced epinephrin, this salt fell out of a hot, weak, alcoholic solution in the form of large, broad and very thin crystalline plates. On attempting to recrystallize it, however, it fell out in the form of small spherical nodules. Since this time I have had no occasion to repeat the work.

Takamine has thus far failed to describe his methods or to give any analytic data as to the elementary composition of adrenalin. Such an important characteristic as its power to reduce copper sulphate, a property not possessed by the native principle, if known to him was for some reason not stated.

Aldrich, in a recent paper,¹² though like others, unaware of Takamine's method, states that he has isolated the adrenalin of this chemist by a method whose essential points are the use of lead acetate for the removal of inert substances, as originally advised by Holm,¹³ and later by v. Fürth,¹⁴ and of ammonia for the precipitation of the free base as originally used by me in the case of reduced mono-benzoyl epinephrin. An important step in this method, of whose significance Aldrich appears to be unaware, is the use of sulphuretted hydrogen for the removal of excess of lead. As already shown, this must effect a reduction, and inasmuch as Aldrich declares his adrenalin to be identical with that of Takamine, it is safe to assume that the acidity of his solutions was not high enough to prevent the occurrence of this reaction.

Both Takamine and Aldrich appear to believe that adrenalin is a pure compound, a true chemical individual. The former has said,¹⁵ "I am now pleased to announce that I have succeeded in isolating the blood-pressure raising principle in a stable and pure crystalline form;" and the latter has stated¹⁶ that he has obtained the compound "in distinctly

crystalline and pure condition;" but in a later section of his paper in which he comments on the close approximation of his formula to that now given for epinephrin, he is less emphatic and gives expression to a doubt by saying¹⁷ "that the difference can be readily explained if we suppose either of the substances to be contaminated with other bodies." The arithmetical mean of the concordant analytical numbers given by Aldrich, shows that the elementary composition of Takamine's adrenalin is represented by:

C = 58.03		C = 57.89
H = 7.20		H = 7.33*
N = 7.66	and by	N = 7.50
O = 27.11		O = 27.27
<hr/>		<hr/>
100.00		99.99

* A misprint occurs in the table as given by Aldrich. The value for hydrogen should be given as above and not 7.23 as given in his paper.

for the identical substance as isolated by himself.

Using these analytical data for the determination of an empirical formula, Aldrich finds that "the simplest body obtainable is represented by the formula $C_9H_{13}NO_3$."

The calculated values for the formula are, however, not placed by the side of the above data for comparison. When these values are calculated, taking O = 16 and whole numbers for H and N as Aldrich has done in calculating his analytical results, the following is the result:

Theoretical for $C_9H_{13}NO_3$.	
C =	59.02
H =	7.10
N =	7.65
O =	26.23
<hr/>	
100.00	

On comparing these theoretical values with those actually obtained by Aldrich, it will be seen at once that the assumed formula does not coincide with the analytical data. In the case of Takamine's adrenalin the mean percentage of carbon as found by Aldrich falls 1% below that required by the formula and in the case of his own compound it falls 1.13%, in the case of one of the two analyses even 1.38%, below the requirements of the formula. This very great deficiency in carbon is the more striking when it is observed how close is the approximation of the obtained hydrogen to that required by theory.

Furthermore, the nitrogen of the compound is estimated by the method of Dumas and the percentage as found is, in the case of Takamine's substance, in exact agreement and in the case of Aldrich's compound falls slightly below the theoretical requirement. Exact agreement with the theoretical requirements is unusual in the employment of this method even when very special precautions are observed, of which

¹¹ Therapeutic Gazette, vol. xxv, p. 221.

¹² American Journ. of Physiol. vol v, p. 457.

¹³ Journ. f. pract. Chem. Bd. 100, (1867), S. 150.

¹⁴ Zeitschr. f. Physiol. Chem. Bd. xxix, (1900), S. 105.

¹⁵ Loc. cit. p. 222.

¹⁶ Loc. cit. p. 458.

¹⁷ Loc. cit. p. 461.

there is no evidence in this case, while an analytical deficiency in nitrogen is in direct opposition to the results of experience with this method, so that both considerations strengthen the conviction that a true formula calls for less nitrogen than does the one proposed by Aldrich.

The great deficiency in carbon that has been pointed out would in itself condemn the assumed formula.

It must be remembered that Takamine and Aldrich are dealing with a substance which they say "was obtained in a distinctly crystalline and pure condition," and they must, therefore, meet the standards universally adopted by chemists for a substance of that character. It is moreover agreed that a strict adherence to these standards is especially necessary in determining an empirical formula based on the analysis of one compound only and unfortified by an analysis of derivatives. In the case of a series of compounds such a deviation from the theoretical requirement may occur in one instance or another of the series as a consequence of drying at too high a temperature or for some reason unexplainable at the time, and under such circumstances the analysis may be allowed to pass.

Not only is the assumed formula inadequate but the case is such that it is impossible to calculate a rational formula that will agree with the analyses given. In other words, adrenalin as analysed by Aldrich is proved by his own data to be a mixture and not an individual substance.

Several possibilities suggest themselves in explanation of this failure to calculate a formula; adrenalin may be simply a mixture of reduced and non-reduced epinephrin; or, it may consist of reduced epinephrin contaminated with ammonium acetate (whose presence is accounted for by the method employed), or it may be contaminated with some one of the numerous nitrogenous bases with which the gland abounds. On any one of these suppositions, the analyses would show a lower percentage of carbon and a higher percentage of nitrogen than is required by the formula for reduced epinephrin, $C_{10}H_{11}NO_3$.

I conclude that the first suggestion is the most probable for the reason that adrenalin possesses a very high degree of physiological activity, as shown by experiments with it in my laboratory, that it has a tinctorial power when treated with ferric chloride practically equal to that of native salts prepared by other methods, and also because it reduces copper sulphate. On this last point, which would give decisive information, no quantitative experiments have been made.

At the time when the colorimetric comparisons here alluded to were made, I had not as yet perfected the method which will presently be described, and I would not have it assumed that there was no chance for error in these estimations or that blood-pressure tests are anything more than a guarantee of an approximate degree of purity. In estimating the value of the several suggestions above made to account for Aldrich's inability to assign a correct rational formula, it must be borne in mind that a substance which falls out of solution as a finely divided, microcrystalline powder

is very apt to carry down foreign substances and to hold them with tenacity.

It must be apparent that both suprarenin and adrenalin are nothing but modifications of the substance that I have called epinephrin. All these substances behave in the same manner toward solutions of silver nitrate and other oxidizing salts, all alike form iron and other metallic derivatives, all are equally capable of being acetylated, benzoated, etc.; all can be made to show the characteristic autoclave effect, all yield with alkalis, a peculiar basic substance of a coniine-piperidine-like odor and a black pigment of acid character, and have many other characteristics in common.

The formula assumed for suprarenin has been shown to be entirely inadequate, and I entertain the hope that a better purification of adrenalin ($C_9H_{13}NO_3$), and an analysis of its derivatives will result in a closer approximation to my formula, $C_{10}H_{11}NO_3$. In order to give additional grounds for this formula I may here present the results of an analysis of a sulphate of the phenyl carbamic di-ester of reduced mono-benzoyl epinephrin. This compound, which had passed through five previous chemical stages, a fact which gives additional guarantees of individuality, was briefly described in the American Journal of Physiology, March, 1900 (Proc. Amer. Physiol. Soc., p. xvii). Although only one analysis was made, the results are given on the assumption that they are of value even without duplicates, inasmuch as they coincide fairly well with those obtained for the whole series.

Found.	Calculated for $[C_{17}H_{15}NO_4 \cdot 2(CO \cdot NH \cdot C_6H_5)]_2H_2SO_4$
C = 63.14	C = 63.70
H = 4.89	H = 4.45
H_2SO_4 = 8.46	H_2SO_4 = 8.39

As the material used in the preparation of this ester was the bi-sulphate of mono-benzoyl reduced epinephrin ($C_{17}H_{15}NO_4$) calculation easily leads to $C_{10}H_{11}NO_3$ as the formula for the free reduced base.

OUTLINE OF A METHOD FOR THE QUANTITATIVE ESTIMATION OF EPINEPHRIN BY COLORIMETRIC COMPARISONS.

It has been known since Vulpian's time that aqueous or dilute alcoholic extracts of the suprarenal gland give a pure emerald green color with ferric chloride. When this test is made with pure epinephrin or with one of its salts, it is found that the color persists for a very brief period only, rapidly giving place to a pink and later to a dark brown shade.

The fleeting nature of this color reaction has made it impossible hitherto to base a quantitative method of estimation upon it. I have now made the observation that the addition of an equal quantity, or, better, of an excess of potassium benzene thio-sulphonate to a solution containing epinephrin, results in a very prolonged fixation of the green color produced by ferric chloride. Solutions thus treated have maintained their tint unaltered even after an exposure of several days to the air of the laboratory.

This salt similarly fixes the green color produced in solutions of pyrocatechin by the addition of ferric chloride, and the reaction probably applies also to related compounds. An alcoholic ether solution of pyrocatechin which contained enough water to hold the added thio-sulphonate in solution, maintained the green color conferred upon it by ferric chloride, in all its intensity after standing in my laboratory for four months.

It may be remarked in this connection, that it now becomes possible to isolate and study this ferric compound of pyrocatechin.

It will readily be seen that a quantitative colorimetric method for the estimation of epinephrin, pyrocatechin and other compounds may be based on the peculiar stability which is conferred upon their ferric compounds by potassium benzene thio-sulphonate. I have not yet had time to elaborate the details of the method, or to determine the range of its applicability, and I shall not here enter upon an explanation of the chemical reaction involved.

SUMMARY.

The following conclusions, drawn from the present paper, are here given, together with a few points whose tenability is easily established by a perusal of my former papers.

1. Epinephrin in its native state easily reduces silver nitrate and other metallic salts, but fails to reduce Fehling's solution. On being treated with hydrogen sulphide or with hydrochloric acid and tin in the proper medium, or on saponification of its benzoyl or acetyl derivatives in the autoclave, it becomes an energetic reducing agent for alkaline copper solution and causes an abundant precipitation of cuprous oxide in the boiling mixture. This change in respect to copper sulphate is accompanied by an alteration in other properties. The substance is now not quite so easily oxidized on the addition of dilute ammonia, and is more easily crystallized.

2. The commercial preparation known as adrenalin also reduces copper sulphate. It is apparent from the analytical data furnished by Aldrich that this substance is a mixture and not a chemical individual. The proposed formula

$C_9H_{13}NO_3$, does not coincide with the analytic data furnished by Aldrich, and no rational formula is deducible from them. Adrenalin is very probably chiefly a mixture of native and reduced epinephrin, containing traces of foreign substances rich in nitrogen. It is hoped that a better purification together with an analysis of its derivatives, will result in a closer approximation to the formula $C_{10}H_{11}NO_3$, which applies to reduced epinephrin as contained in my series.

3. The series of epinephrin compounds described by the writer in previous papers; have one and all retained a single benzoyl radicle, in consequence of the incomplete saponification of the original benzoyl derivative. This could not be determined with certainty until the substance was isolated by methods which avoided the process of benzoating. The epinephrin, $C_{17}H_{15}NO_4$, of my former papers was therefore in reality mono-benzoyl epinephrin, and in consequence of its ability to reduce alkaline copper sulphate it may further be designated, reduced mono-benzoyl epinephrin.

4. Elimination of the retained benzoyl radicle (C_6H_5CO), and substitution of the displaced hydrogen atom leads to the formula $C_{10}H_{11}NO_3$, as an adequate empirical expression for reduced epinephrin, at least for epinephrin as reduced by saponification in the autoclave.

5. My own work, as also that of Aldrich, shows that the statement of v. Fürth that the substance under discussion is either tetrahydrodioxypyridin $C_5H_9NO_2$, or dihydrodioxypyridin $C_5H_7NO_2$, is no longer tenable.

6. Reduced epinephrin is capable of taking up four acid radicles. This is shown in an earlier paper in which it was demonstrated that mono-benzoyl epinephrin is capable of taking up three acetyl groups. Mono-benzoyl epinephrin is also capable of forming a phenyl carbamic di-ester, and probably even a tri-ester on more vigorous treatment with phenylisocyanate ($CO.N.C_6H_5$).

7. Potassium benzene thio-sulphonate, $KS.SO_2C_6H_5$, added to a solution of epinephrin fixes the emerald green color which appears on the subsequent addition of ferric chloride. A colorimetric quantitative method may be based on this reaction. The ferric compound of pyrocatechin is also permanently fixed in its tint by this sulphonate, and the reaction possibly applies to related compounds.

OSTEITIS DEFORMANS WITH REPORT OF A CASE.*

BY ARTHUR W. ELTING, M. D.,

Attending Surgeon, The Child's Hospital.

(Chief of the Surgical Clinic, The Albany Hospital),

Albany, New York.

To Sir James Paget belongs the credit of having described in a clear and concise manner an unusual form of disease

* Read before the Medical Society of the County of Albany, Nov. 13th, 1900.

characterized by hypertrophy and deformity of certain of the bones of the skeleton. To this disease he gave the name of osteitis deformans.

Paget's¹ original communication was presented to the med-

ical and surgical society of London in 1876 and included a report of five cases observed by himself. Certain cases reported in earlier times as partial or local osteomalacia were undoubtedly cases of osteitis deformans, as, for instance, cases reported by Saucerotte² in 1801, Rullier³ in 1812, Scoutetten⁴ in 1841, Wrany⁵ in 1867, and Mosetig⁶ and Wilks⁷ in 1868. Certain of these cases Paget himself recognized from the description given as being in all probability osteitis deformans.

Czerny⁸ in 1873 first introduced the term "osteitis deformans" in connection with a case of gradual spontaneous development of a curvature of the lower legs. Benno Schmidt,⁹ in 1874, used the term in connection with a case of spontaneous development of curvatures of the tibia and femur, and Volkmann,¹⁰ in 1874, used the term in a similar case in which the curvature was confined to the tibia. The points of differentiation from osteomalacia emphasized by these observers were the inflammatory symptoms manifested by the involved bones and especially the pain.

The term "osteitis deformans" was thus not a new one, but it was Paget who first applied it to the peculiar disease entity which he described. Since Paget's original communication a considerable number of characteristic cases have been reported. Up to 1890 Paget himself had seen 23 cases, far more than has fallen to the lot of any one else to observe.

More cases of osteitis deformans have been reported from Great Britain than any other country, but this is probably due to the fact that the interest aroused by Paget in the subject has led to a more careful search for such cases. The next greatest number of cases of osteitis deformans have been reported from France, where the work of Richard,¹¹ Thibierge,¹² Joneheray,¹³ and others has aroused especial interest in the condition. A few cases have been reported from Germany, Austria and Italy. So far there appear to have been seven cases of osteitis deformans reported from America. The first case was that of MacPhedran,¹⁴ of Toronto, reported in 1885. The second was reported by Gibney,¹⁵ of New York, in 1890. The third by Maekensie,¹⁶ of Toronto, in 1891. The fourth and fifth by Taylor,¹⁷ of New York, in 1892. The sixth by Herwisch, of Philadelphia, in 1896, and the seventh by Watson,¹⁸ of Baltimore, in 1898. Watson's case was more characteristic than any of the former ones reported from this country.

Many of the cases reported have been accompanied by pathological reports, the most valuable contributions having been made by von Recklinghausen,¹⁹ Stilling,²⁰ Paget and Butlin.²¹ von Recklinghausen called the disease osteomyelitis fibrosa and demonstrated its identity with certain cases of local osteomalacia of earlier writers.

The involvement of the different parts of the skeleton varies in different cases. All of the long bones, the clavicles, the flat and short bones, and especially the vertebrae, may be more or less affected. The tibia appears to come first in the order of frequency of involvement and in some cases is the only bone involved. Next in order of frequency comes the skull which is also in certain cases alone involved, and the

vertex is more commonly affected than the base. The femur appears to come next while the frequency of involvement of the other bones of the skeleton varies greatly. The disease rarely attacks the bones of the face, although cases are reported in which the superior and inferior maxilla as well as the zygoma have been affected.

Based upon Butlin's microscopic studies of the first case, Paget laid the chief emphasis upon the inflammatory absorption of the bone associated with the formation of lacunae. He believed the fibrous character of the bone marrow to be the result of the long duration of the inflammatory process. He also called especial attention to the apparently increased vascularity of the affected bones as evidenced by the enlarged blood-vessels of the periosteum and bone. Many other observers do not share the views advanced by Paget and Butlin as to the inflammatory character of the disease. Stilling, in his report of three carefully studied cases, discusses the pathological process and states that the disease begins beneath the periosteum and gradually involves the more central portions of the bone. There is at first an absorption of the bone with the formation of Howship's lacunae, Haversian spaces and perforating canals. In these changes Stilling believes the process resembles that which occurs in ordinary rarifying osteitis. In addition to the absorption, however, as in all chronic inflammations of bone, there is a new formation of bone, partly in the marrow and partly beneath the periosteum. Stilling states that both processes appear to go on at the same time and that the newly-formed bone may again be absorbed. The absorption appears to gradually grow less while the new formation continues, and thus the bones come to present most marked modifications, both of the internal structure and external appearance. They become thick and misshapen.

The new-formed bone remains for a long time uncalcified, and is, therefore, soft and has a tendency to yield under the body weight. Sometimes, however, there may be more or less calcification of the new-formed bone, as evidenced by calcified areas demonstrated here and there.

The tibia and femur become bent anteriorly or laterally or both; the angle of the neck of the femur to the shaft is changed; the vertebral column presents abnormal curvatures and the lower part of the skull is pressed upward toward the cranial cavity.

Laneereaux²² believes the pathological process to be characterized by an absorption of bone followed by a process of bone formation, and that the latter is merely a reparatory process.

Against the view that the bone formation in osteitis deformans is merely a regenerative process, Silecock²³ and von Recklinghausen have urged that the new formation does not occur upon the side of the concavity, and furthermore that the thickening of the bone can be demonstrated at the very beginning of the disease. Mere quantitative variations in the absorption and formation of bone in osteitis deformans do not explain the condition, but the quality of the bone formation must also be considered.

According to von Recklinghausen's investigations, the changes occur in the following manner: At first there is a simple osteomalacia with a marked reduction of the cortical substance of the bone, as a result of which the bones become bent. Following this an inflammatory process develops in the malacic areas which is characterized by the transformation of the fatty and lymphoid marrow into fibrous tissue, from which a compact network of bone develops which contains much fibrous tissue, and which remains uncalcified for a long time. Where the disease has existed longest this process may lead to a complete disappearance of all the old bone tissue. From this result the great modifications of the bony structure.

The fact that the anatomical findings of all the writers do not agree is probably because the cases have been studied at different stages of the disease. In cases in which the progress of the disease is a slow one, as in Paget's first case, as well as in the cases of so-called local osteomalacia of early writers, the most characteristic feature is the presence of a finely porous bone tissue situated in the cortex of the long bones and occasionally in the medulla, as well as in the spongy tissue of the short and flat bones. These areas in some places present little or no calcification, while in other places there is a marked deposition of calcium salts, and at times one may encounter areas of an ivory hardness which might be considered as evidence of a healing process.

In the more advanced stages of the disease the bone marrow presents the appearance of a pale or reddened fatty marrow. In cases developing rapidly, especially those in which there is a general distribution of the process over the skeleton, the new bone and the fibrous bone marrow are much in evidence. The porous bony tissue may be found to have replaced the compact cortex or to have developed extensively in the medulla, both in bones which present little or no outward evidence of involvement, as well as in those presenting tumor-like enlargements and marked deformity. In this fashion tumors resembling fibromata may develop in which there may be little or no bone formation. This process explains the lengthening that sometimes occurs in the deformed long bones.

von Recklinghausen has demonstrated that in addition to transformation into osteoid tissue, the fibrous marrow may manifest either regressive or progressive changes. The regressive changes may lead to the smooth walled multilocular cysts, containing either a serous or gelatinous substance and occurring chiefly in the long bones, but also occasionally seen in the skull. The progressive changes lead to the formation of small brownish-red tumors with the structure of pigmented giant cell sarcomata, which also have their situation in the long bones, but are always surrounded by the fibro-osteitic tissue from which they take their origin. The existence of cysts in the fibrous medulla of certain cases hitherto supposed to be instances of local osteomalacia makes it probable that these were cases of osteitis deformans. Hirschberg,²⁴ in such a case, described in the neighborhood of the cysts a small giant cell sarcoma. Certain of the cysts of bones described in other connections may have their origin in

a condition of osteitis deformans. The cysts and sarcomata in cases of osteitis deformans seem to indicate the situation of the earliest changes in the medulla.

von Recklinghausen has especially emphasized the rôle played by the action of so-called physiological concussion in the determination of the localization of osteitis deformans, as evidenced by the tendency to involvement of the long bones of the extremities. The newly-formed fibro-osteitic tissue is most marked at the diaphysis of the bones which are the points subjected to the greatest physiological concussion. von Recklinghausen is also of the opinion that the frequent involvement of the skull may find its explanation in disturbances of circulation, especially arterial congestion, resulting from the action of mechanical and thermic influences.

The two most important factors then concerned in the production of the deformity of the bones are:

- (1) An hypertrophy of the bone.
- (2) A relative softening which accompanies the onset and which appears to be only temporary, being followed usually by induration.

Chemical analysis has shown that the phosphorus is but slightly diminished in the affected bones. The organic matter of the bone as a whole is slightly above normal, while the inorganic is slightly below normal.

In some of the cases reported careful blood examinations have been made, but these have been negative in every instance.

Concerning the etiology of osteitis deformans practically nothing is known. Sex and heredity do not seem to play a rôle. The venous dilatation seen in certain cases may be an etiological factor, although this seems improbable.

Richard, in his thesis published in 1887, advanced the view that osteitis deformans is closely related to arthritis deformans. Although in a few instances the two diseases may have co-existed, there is no reason for assuming any definite relationship between them. Richard attempted to distinguish three varieties of osteitis deformans.

(1) Those cases in which there are no lesions of the joints, *i. e.*, the type described by Paget.

(2) Cases in which both the shafts and joints are affected.

(3) Cases in which arthritis deformans is associated with osteitis deformans.

Although frequently assumed, there has never been any positive proof adduced to show that osteitis deformans is dependent upon lesions of the peripheral or central nervous system. In a few cases, lesions of the central nervous system have been demonstrated at autopsy, as in the two cases of Giles de la Tourette and Marinesco²⁵ and in the case of Levi,²⁶ in all of which marked degenerations of the tracts of the spinal cord were demonstrated. It is, however, probable that these were mere coincidences, for in many cases the spinal cord, sympathetic system and peripheral nerves have been carefully studied without the discovery of any lesion that would explain the disease.

Lancereaux adheres to the view that diseases of the nervous system play a rôle in the etiology of osteitis deformans,

basing his ideas upon the fact that the bones present the same characteristics as are seen in the bones of an extremity after section of the nerve governing that extremity.

Schiff²⁷ has demonstrated that section of the sciatic and crural nerves in young dogs is followed in three or four months by a thickening of the tibia, fibula and bones of the feet. The medullary canal is obliterated and osteophytes develop upon the surface of the bones. In older animals an osteoporosis develops at first, and after a year or so an hypertrophy of the bone occurs. These experiments have been confirmed by Vulpian and Philipeaux,²⁸ but Vulpian calls attention to the fact that changes in the bone do not invariably follow section of the nerve.

The consensus of opinion seems to be that there is no definite relationship between diseases of the nervous system and osteitis deformans.

The disease usually develops in individuals past forty years of age and most frequently begins in the tibiae or the bones of the skull. Gradually other bones may become affected, but there appears to be an especial tendency to involvement of the long bones of the lower extremities, the skull and the clavicles.

The affected bones increase markedly in size and appear to be more or less nodular; the firmness of the bones is diminished and those subjected to the action of weight or pressure become deformed. In characteristic cases the parietal bones become more prominent, the occipital bone is distinctly enlarged, the temporal fossae are less marked and the frontal bone overhangs the face. The curves and size of the clavicles are increased. The thorax assumes a globular shape. The arms appear to be relatively too long and frequently show deformities, especially the forearms. Dorsal kyphosis is not uncommon. Scoliosis is, however, quite rare. The pelvis is often enlarged and the brim is everted. The trochanters are higher than normal, as a result of their hypertrophy and the more horizontal position of the neck of the femur. The femurs are hypertrophied and curved, the convexity being outward. The patellae may be hypertrophied. The tibiae are massive with rounded edges and present curvatures with the convexity outward and forward. The legs are usually involved symmetrically, although the process may affect only one or a few bones and remain localized in them. In advanced cases the posture of the patient is characteristic. As a result of a bending of the vertebral column and lower extremities the individual becomes shorter. The apparently excessively long arms, the unsteady gait, the bowed knees, the round shoulders and the head inclined forward give to the individual somewhat of an ape-like appearance.

More or less pain often accompanies the development of the earliest deformities, and it may also be very intense before any deformity has occurred. At times the pain manifests more or less of a periodical character, occurring at night or after fatigue.

The pain of onset is usually the most severe, occurs both day and night and either spontaneously or as a result of pressure, and may be mistaken for rheumatism or neuralgia. As

the disease progresses the pain tends to become less severe and may only be caused by exercise or humid weather.

Durverney in 1757, in discussing the pains of the initial stages of rachitis, believed them to be due to a distension of the periosteum, and this would also seem to explain the pains of osteitis deformans. As has already been remarked, the pains in osteitis deformans are most pronounced during the early stages of the disease when the bones are undergoing hypertrophy. Later on, when the hypertrophic process seems to be arrested, the pains are apt to disappear.

As for the general pains, abdominal, lumbar, etc., the neuralgia, migraine and vertigo which occasionally occur, they may be explained by the pressure of the hypertrophied skull or vertebrae upon the brain, cord or nerves.

On the other hand there are certain cases in which pain does not occur in spite of the very evident lesions of the bones. This may be explained by a very slow development of the disease in which instance the periosteum would be but slowly and slightly distended.

Joneheray distinguishes two varieties of osteitis deformans: (1) a painful variety and (2) a painless variety. The painful variety is the more frequent and presents the more marked lesions, while the painless variety develops more slowly and with less intensity. The progress of the disease is slow, from five to fifteen years being usually necessary to produce the maximum changes. The condition of the patient is usually very satisfactory, the general health as a rule is good and there is nothing in the nature of the disease which need necessarily shorten life. Among the complications that may intervene may be mentioned a slight tendency to fractures of the affected bones. The occurrence of visceral carcinoma in association with osteitis deformans has also been noted. It is doubtful, however, whether this is more than a mere coincidence.

Among the conditions from which osteitis deformans is to be differentiated may be mentioned: (1) Simple hyperostoses, (2) Hyperostoses as a result of an excessive blood supply, (3) Hyperostoses of elephantiasis, (4) Inflammatory or traumatic hyperostoses, (5) Senile osteoporosis, (6) Osteomyelitis, (7) Syphilitic hyperostoses, (8) Hydrocephalus, (9) Chronic rheumatism, (10) Acromegaly, (11) Pulmonary osteoarthropathy, (12) Leontiasis ossea, (13) Rachitis, (14) Osteomalacia.

Osteomalacia presents certain points of resemblance to osteitis deformans. In osteomalacia, however, the absorption process is much less marked and furthermore in osteitis deformans one does not find areas of decalcification of the bone tissue which is the most characteristic feature of osteomalacia. It must, however, be admitted that a certain proportion of the tissue in osteomalacia is new formed.

Osteitis deformans differs from rachitis in that the latter is a disease of the growing bone in which changes occur chiefly in the zone of growth and the ends of the bone; such, however, is not the case in osteitis deformans.

Leontiasis ossea is a disease of younger individuals in which there are marked hyperostoses not only of the bones of the

skull but also of the face. This marked thickening of the bones lessens the capacity of the skull cavity and narrows all the fissures and openings of the skull, as a result of which there may be more or less marked disturbances of the cranial nerves, and deafness and loss of smell may ensue. Anatomically there is a marked sclerosis of the bone tissue, all of which characters serve to differentiate the disease from osteitis deformans.

Acromegaly is also a disease of younger individuals characterized by an enlargement of the bones of the face while the skull is not involved. There is also an hypertrophy of the bones of the hands and feet without marked deformity and with little or no involvement of the long bones.

The treatment of osteitis deformans consists in relieving the pain and supporting the general health of the patient. There is no known method of arresting the process or preventing the deformities.

In the service of Dr. Morrow and subsequently in that of Dr. Macdonald at the Albany Hospital it has been possible to carefully study the following case:

J. H. G., age 45; nativity, England; occupation, book-keeper.

Complains of fracture of the right arm and bowing of legs.

Family History.—Father died of heart disease at the age of 65. Mother died of uterine trouble, at the age of 55. Six brothers, all dead, causes unknown. Four sisters, all dead, three in infancy, one of Bright's disease. No family history of any trouble similar to the patient's present condition.

Personal History.—Usual diseases of childhood. Had a fever for two weeks, at 17 years of age, which he thinks was typhoid. No history of malaria or pneumonia. His general health has always been good until the onset of his present trouble. Has taken alcohol moderately in the form of beer, wine and whiskey. Denies syphilis and gonorrhœa. Smokes and chews moderately. Has been a rather hearty eater. Has never done much hard work and has never been exposed to the weather. No history of bowel or bladder trouble, and no history of previous fractures.

Present Illness.—Began in June, 1888, with a sharp pain in the left knee. Prior to this time the patient had never had any severe pain in the bones or joints. This pain lasted about 12 days, during which time the patient was in bed. The knee was somewhat swollen. The patient says he does not think he had any fever. After this attack he was perfectly well for about four years. In February, 1892, the patient had a second attack of pain in the left knee, accompanied by some swelling of the joint. In a few days the other knee joint, both ankle joints, both shoulders, both elbows, both wrists and hands, as well as the vertebral joints became involved. The joints were swollen but the patient says he had only slight fever and no sweats. He was in the St. Peters Hospital for about four months and appeared to have recovered completely, there being no further trouble in the joints. The diagnosis made at that time was articular rheumatism. The patient returned to work in July, 1892,

but says that about that time he first noticed that his legs, which had always been perfectly straight, were becoming slightly bowed. The patient thinks the bowing at first was outward, and that the bowing was more marked in the left leg. This bowing of the legs has gradually increased up to the present time, and during the past three or four years he has noticed that an anterior bowing of the legs has also developed, which has gradually increased, but more slowly than the outward bowing. He has had more or less pain in the bones of the legs and in the knee joints during the past eight years. He has also had some pain in the bones of the arms and in the other joints of the body, but his trouble has been confined mainly to the bones of the legs and the knee joints. He says that the pains are usually of a sharp, shooting character, but there have also been dull pains in the bones and joints. The pain has never been severe enough to incapacitate him for work since the attack in 1892. The motion of the joints has not been impaired, except during the two attacks mentioned and the patient has been able to walk and get around without difficulty. The patient says that his height before the onset of his present illness was five feet, seven inches; his present height is five feet, one and one-fourth inches. About 1892 he thinks his head began to enlarge so that he was compelled to wear a larger sized hat. He says in 1892 he wore a $7\frac{1}{8}$ hat, but that during the four years from 1892 to 1896 he was compelled to gradually increase the size of his hat to $7\frac{3}{4}$, which size he has worn since 1896. He has never had severe headache nor any special pain in the bones of the skull. His general health has been good and he has attended to business regularly. He has never noticed any bowing or deformity of the arms.

On April 2, 1900, the patient fell two and one-half feet; struck on the shoulder and sustained a fracture of the neck of the humerus. He has been unable to use the arm since. He came directly to the Albany hospital, where the arm was put up in splints and kept in splints and plaster until June 16th, without any evidence of union between the fragments. On June 16th an attempt was made to wire the fragments, but owing to the much softened condition of the bone the operation was very unsatisfactory. At this time a fracture just above the condyles of the humerus was discovered which was undoubtedly produced during the operation and which demonstrated the friable condition of the bone. The arm was put up in plaster which was removed on July 2d, at which time there was a slight evidence of union. On July 16th, examination of the arm showed that union had taken place at the sites of both fractures. Examination on August 2d, showed that the union was fairly firm with a moderate amount of callus and a slight deformity at the site of the lower fracture. The elbow, wrist, metatarsal and phalangeal joints were so stiff that movement of the forearm, wrist or fingers was impossible.

Physical Examination.—Fairly well developed, somewhat emaciated man. The shoulders are somewhat stooped, due to a slight dorsal kyphosis. Skin and mucous membranes of good color. Tongue clean, protruded in the median line.

Pupils midwide and equal, react to light and accommodation. Chest somewhat barrel-shaped. The sternum is protuberant. The right clavicle is distinctly enlarged and somewhat roughened, the edges are rounded. Left clavicle is slightly enlarged. Percussion note over the chest hyperresonant. Breath sound clear. Pulse 72 to the minute, regular in rate and rhythm, of fair volume and low tension. The wall of the artery is palpable.

Heart.—Area of cardiac dullness normal. On auscultation a soft systolic murmur is heard at the apex following the first sound, not transmitted to the axilla. Second sound is clear at the apex. Heart sounds are clear at the base.

Abdomen negative. Genitalia negative. Superficial and deep reflexes normal. No clonus.

Viewed anteriorly the skull appears fairly symmetrical. There is a distinct massiveness and prominence of the forehead, the frontal and parietal bones being apparently much enlarged. There is a striking disproportion between the size of the head and the face. Viewed posteriorly there is a distinct asymmetry of the skull produced by an irregular enlargement of the occipital bone, which presents irregular prominences. On palpation the frontal, occipital and both parietal bones appear to be distinctly thickened and enlarged. The thickening and enlargement are most marked in the occipital bone. The external surfaces of these bones are somewhat irregular; they are very firm, and the scalp covering them appears to be normal. No tenderness can be elicited on pressure over these bones. There is no apparent enlargement or asymmetry of the bones of the face. The teeth are somewhat decayed, but regular.

Measurements of the Skull.—From glabella to occipital protuberance $21\frac{1}{4}$ cm.; bi-parietal diameter of skull 16 cm.; bi-temporal diameter of skull $15\frac{1}{4}$ cm.; greatest transverse diameter of skull is 17 cm. in a plane 2 cm. posterior to external auditory meatus; circumference of skull $62\frac{1}{2}$ cm.

There is a most marked bowing of the legs, the bowing of the left being somewhat more marked than that of the right. When the patient stands erect with the heels together there is a distance of $4\frac{1}{2}$ cm. between the internal malleoli and $16\frac{1}{2}$ cm. between the internal condyles of the femurs. The bowing outward is most evident in the lower portion of the femurs; somewhat less evident in the upper portion of the tibiae. There is also a well marked anterior bowing of both femurs. Both the anterior and the outward bowing are most marked in the left femur. On palpation both femurs are found to be distinctly enlarged throughout their entire extent. The surface of the bones is somewhat irregular and roughened but very firm. The enlargement of the trochanters and the lower extremities of both femurs is most striking, although there is also evident enlargement of the diaphyses. The circumference of both legs at the condyles of the femur is $34\frac{1}{4}$ cm. Both tibiae present most marked enlargement, especially in the upper portion; and are roughened and irregular but very firm. Both fibulae appear normal, except that they have participated in the bowing.

Pressure over the femurs elicits some tenderness, which apparently is not localized in any particular part of the bones. In none of the involved bones is there any evidence of tumor formation. Radiographs of both femurs and both tibiae show marked enlargement of the bones associated with irregularities of contour. External rotation and abduction is slightly limited in both hip joints. Other motions at the hip joints are normal. The motions in the knee joints are normal. The scapulae are normal. The left humerus is straight and apparently normal. The right humerus presents a distinct thickening in the region of the surgical neck due to a callus formation, and a slight deformity just above the condyles of the humerus, due to a slight anterior displacement of the upper fragment of the humerus, and the presence of a moderate amount of callus. Union of the fragments both at the surgical neck, as well as above the condyles of the humerus, is firm. Both the radii and both ulnae are normal. The bones of the hands and of the feet are normal. The vertebrae are normal.

The muscles of the entire body, but especially of the legs are atrophic. There is no evidence of involvement of the central or peripheral nervous system.

The most prominent characteristics of this case, then, are an extensive hypertrophy and bending of both femurs and both tibiae, an hypertrophy of the frontal, occipital and both parietal bones, and an hypertrophy of the right clavicle, together with fracture of the right humerus which is evidently involved in the process, although not manifesting any evident hypertrophy.

In conclusion it may be said:

(1) That osteitis deformans is a chronic disease of the bones which develops in middle life or later.

(2) That the disease is of more frequent occurrence than generally supposed.

(3) That the onset is insidious sometimes in a single bone, but usually manifesting a tendency to symmetrical involvement of the bones.

(4) That there is an especial tendency to involvement of the tibia and femur as well as the frontal, occipital and parietal bones.

(5) That it attacks both sexes and does not appear to be related to any constitutional disease.

(6) That the etiology is not understood.

(7) That it requires from five to fifteen years to reach its maximum development.

(8) That it is characterized by hypertrophy and deformity of the bones involved, either with or without pain.

(9) That it is characterized microscopically by a rarifying osteitis combined with new bone formation.

(10) That the duration of the disease is indefinite, and that the disease has but comparatively little influence upon the general health, and furthermore that it is not a direct cause of death.

(11) That treatment must be purely symptomatic.



FIG. 1.



FIG. 2.



Skiagraph of Left Femur.

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- (23) Silcock. *A case of osteitis deformans*. *Pathol. Soc. Transactions*, Vol. 36. p. 383. 1885.
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- (26) Levi. *Un cas d'osteite deformante de Paget*. *Nouv. Iconogr. de la Salpêtrière T. x* p. 113, 1897.
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TUBERCULAR DACRYOADENITIS AND CONJUNCTIVITIS, CONTAINING THE REPORT OF A PROBABLE CASE ENDING IN SPONTANEOUS RECOVERY AND A REVIEW OF THE PREVIOUS LITERATURE ON TUBERCULAR DACRYOADENITIS.

BY EDWARD STIEREN, M. D., Pittsburg, Pa.,
*Assistant in Ophthalmology, Medical Department, Western
 University of Pennsylvania.*

Twelve years ago Cornet made the declaration that at least one-third of all mankind are, or have been, affected with tuberculosis, not including in this sweeping assertion tubercular invasion of the bones and joints, of the skin and glands, and the various hidden depots of the disease. In 4250 successive autopsies made in Breslau in the year 1893 gross lesions of tuberculosis were found in 1393, or one-third of all the cases. Brouardel found characteristic lesions in seventy-five per cent of his cases at the Paris Morgue.¹

Notwithstanding the great prevalence of tuberculosis in the human race, the eye appears to enjoy a greater freedom from tubercular invasion than any other part or organ of the

body. Thus, among 2100 ophthalmic cases observed in hospital and private practice by Grant, not one was diagnosed as being directly due to the action of the tubercle bacillus.²

In 1867, Virchow considered the conjunctiva immune to tuberculosis and in 1870 the first cases of tuberculous conjunctivitis were reported.³

This comparative immunity of the eye to tubercular invasion is due in part to the facts that the eye is almost constantly exposed to a lower degree of temperature than that in which the tubercle bacillus thrives; is very often exposed

¹ Whittaker, *Tuberculosis*. *American Text-Book of Applied Therapeutics*. 1896.

² Grant, L. *Observations on the relative frequency of tubercular diseases of the eye*, *Caledonian Medical Journal*. Glasgow, 1899-1900, iv, 50-55.

³ Grunert. *Archives of Ophthalmology*, xxviii, 1899.

to the direct sunlight; is constantly bathed in and flushed by the tears; and expulsion of germs from the conjunctival sac is aided by the movements of the lids. To this may be added the fact that the epithelial structure of the exposed parts of the eye (epithelium resting on a basement membrane), affords the bacillus very little opportunity for invasion and growth.

Grunert⁴ is pleased to regard tuberculosis of the conjunctiva as a local disease. Van Duyse⁵ regards tuberculosis of the lachrymal gland as hematogenous. Lodato believes tubercular invasion of the lachrymal gland to be ectogenous.⁶

Of all the structures or adnexa of the eye, the lachrymal gland enjoys the greatest freedom from disease.

William Lawrence in over 40,000 eye cases in the Clinic at Moorfields did not find a single affection of the lachrymal gland.

Acute dacryoadenitis was first described by Gayet in 1874.

Chronic dacryoadenitis (better known to the earlier ophthalmologists than the acute form), although still quite rare, occupies a place in pathology, being due usually to either small-pox, mumps, influenza, leucoeythæmia, syphilis or chronic trachoma.⁷

Tubercular disease of the lachrymal gland is one of the rarest of eye affections, twelve cases being on record in the Index Medicus and in the Catalogue of the Library of the Surgeon-General, U. S. Army. De Lapersonne⁸ describes a woman who came to him for the relief of a ptosis and a swelling at the upper outer angle of the orbit of the right eye which had existed for three months. Tuberculosis was not at first suspected although the patient had previously had a cough with hæmoptysis and fever, and had lost in weight. Treatment had relieved her of these symptoms, and on presentation only a little rough breathing could be heard over the left apex. On palpating the lid, the swelling was found to consist of a tumor immediately under the skin, of fibrous consistency and irregular outline. It was extirpated, microscopical examination showing it to be without doubt tubercular in structure. Erlich's stain did not demonstrate tubercle bacilli. L. Müller⁹ reports two cases. One, a fourteen-year old patient in whom the condition had existed for four years. He presented himself with a redness of the upper right lid and a swelling of the outer superior margin of the orbit. Microscopical examination of the extirpated tumor showed it to be typically tubercular with tubercle bacilli present in great numbers. Müller's second case was a forty-year old man, the clinical picture being much the same as in the previous case. A tumor about the size of a hazel-nut occurred on the left side, lay quite deeply, and was

freely movable. Microscopical examination showed typical miliary tuberculosis and tubercular infiltration, with some few tubercle bacilli present. Baas¹⁰ reports two cases. The first, a sixty-nine year old man with no previous history of tuberculosis. For six weeks he had observed a gradually growing tumor in the left upper lid. On palpation, a growth the size of a large hazel-nut could be felt, of elastic consistency, smooth, and extending almost to the outer canthus, interfering with external movement of the eye-ball. The extirpated tumor proved to be typically tubercular, though no tubercle bacilli could be found in the tissues. Baas' second case was that of a thirty-two year old man who since childhood had been affected with nasal catarrh, his nose becoming gradually less pervious to air. A growth was removed from his nose and diagnosed tubercular. For three months the right eye had been red, with pain in the region of the lachrymal gland and a growing tumor in this region from which he sought relief. Tumor was the size of a cherry, composed of small nodules, was freely movable, and could be mapped out on all sides. It was hard, and on its outer aspect a smaller, flatter hard mass could be felt. The eye-ball was undisturbed in its movements, and the ocular conjunctiva was much injected. A quarter of the extirpated tumor in a horizontal section had the appearance of normal lachrymal gland. The outer three-quarters was a hard, compact mass, in which with the naked eye large and small nodules could be seen, microscopically proving to be tubercles. Examination for tubercle bacilli was negative. Süsskind, J.,¹¹ reports a girl twenty-one years old, who for about two and one-half years had observed a tumor in her left upper lid. For a year the tumor had not increased any in size. The skin of the lid over the tumor had the appearance of telangiectasis with marked ptosis. On superficial palpation the tumor appeared soft and spongy, but on firm pressure a hard mass could be felt, disappearing under the rim of the orbit. The tumor appeared to have a pulsation, due to the well formed vessels in the lid. Patient had enlargement of the cervical, inguinal, and preauricular glands. The lachrymal gland and the preauricular glands were removed, and in them, on microscopical examination, were found epithelioid and lymphoid tubercles, containing tubercle bacilli.

Süsskind thinks his case remarkable for the reason that the preauricular glands were affected at the same time with the lachrymal, and because the disease ultimately extended to the parotid gland. Abadie¹² saw a case of double tubercular dacryoadenitis in 1894. Some time later a similar case occurred in the clinic of Prof. Manz in Freiburg,¹³ and one in the practice of Salzer.¹⁴ Ziegler verified the microscopical

⁴ Loc. cit. ⁵ Loc. cit.

⁶ Lodato, G. Tubercolosi primaria dell ghiandola lagrimale. Arch. di ottal. Palermo, 1896, iv, 383-396.

⁷ Baquis, E. Das Trachom der Thränendrüse etc. Beitrag zur path. Anat. und zur allgemein Path. Jena 1896, xix, 406-432.

⁸ Tuberculose prob. de la gland lacrymale. Archiv. de l'ophthalm. 1892, xii.

⁹ Ueber primäre Tuberculose der Thränendrüse. Beiträge zur Chirurgie-Festschrift für Billroth. 1892, p. 144.

¹⁰ Tuberkulose der Thränendrüse. Archiv f. Augenheilk. 1894, Bd. 28.

¹¹ Klinischer und anatomischer Beitrag zur Tuberculose der Thränendrüse. Archiv f. Augenheilk. Wiesbaden, 1896, xxxiv, 221-229.

¹² Axenfeld und Fick, Pathologie des Auges. 1898.

¹³ Über einige tuberkulose Entzündungen des Auges. Munich. med. Wochenschrift. 1895.

¹⁴ Ein Beitrag zur Kenntniss der Tuberculose der Thränendrüse. von Graefe's Archiv, Bd. xl, Abth. v.

diagnosis in the latter case. The tumor was 1.8 cm. long, 1 cm. wide, and quite flat; edges round, irregular in size, and divided into lobes. It had the appearance of a normal gland but on microscopical examination miliary tubercles, abundant round cell infiltration, concentrically arranged around the tubercles were found. Lymphoid tubercles were absent, nor could any tubercle bacilli be found. Lodato¹⁵ found in a fifty-two year old woman a lachrymal gland tumor the size of an almond; hard, nodular, and freely movable, on section proving to be typically tubercular. Tubercle bacilli could not be found in the gland. Van Duyse¹⁶ describes a case of attenuated tuberculosis of the lachrymal glands with spontaneous recovery. A girl, æt. 19, anæmic and serofulous, presented herself with a swelling in the superior lids of both eyes. No pain, inflammation, nor redness. On palpation a tumor of cartilaginous consistency was felt on either side which could be made to disappear under the rim of the orbits. A portion of one was excised for microscopie examination, the clinical diagnosis of sarcoma having been made. Pending the result of this examination the patient was given iodide of potassium in fifteen grain doses, three times daily. She presented herself six weeks later with a total disappearance of all induration in the region of the lachrymal glands. In the meantime microscopical examination of the excised portion of the gland showed it to be tubercular, tubercle bacilli absent. Inoculation in the guinea-pig was negative.

Van Duyse's resumé is as follows: "Tuberculosis of the lachrymal gland should not be considered primary; the infection seems to come from remote parts of the body, being hematogenous. Tuberculosis of the eye can be evolved under an attenuated form and extinguish itself on the spot."

Tikanadze¹⁷ saw a case of tuberculous inflammation of the lachrymal gland in 1897.

The following contribution to the literature on tubercular disease of the lachrymal gland bears many features of Van Duyse's case. Rose M., colored, æt. 13, presented herself in the Eye Clinic of the Medical Department, Western University of Pennsylvania, September 8, 1900, on account of a swelling of both upper lids and an almost constant discharge of matter from the eyes.

Family history.—Rose is the only surviving one of five children, the others having died in infancy; maternal uncle died of consumption, paternal grandmother died in old age and was affected with "cancer of the face" (probably lupus). Both parents living and healthy.

Previous history.—Patient had measles at four years, whooping-cough at six years, and mumps at about ten years of age.

Present illness.—About three months before her appearance in the clinic, patient began to have a cough, more severe at night, accompanied with quantities of yellow expectoration. Has been losing in weight only since that time, and has had

night-sweats almost every night. Menstruation is irregular and scanty. About the same time her parents noticed an increasing fullness and prominence of the upper lids accompanied by a more or less purulent discharge from the eyes. There has been no pain connected with the disorder and no discomfort except a slight burning sensation referred to the outer canthi.

Examination. General.—Patient is a chocolate-colored negress, almost five feet in height and weighs ninety pounds. Is fairly well nourished about the face and neck but shows marked emaciation about the trunk and limbs. Chest expansion, one and one-half inches. Both parotid glands are enlarged, tender, lobulated and movable. Both supraclavicular spaces filled with masses of enlarged glands. Thyroid glands enlarged, right lobe most affected. Dullness well marked with a tone and a half elevation of pitch over right apex. Diminished respiratory murmur and deficient expansion over entire right lung. Roughened breathing, pro-



Bilateral Tubercular Dacryoadenitis.

longed expiration, and subcrepitant râles over right supraclavicular and suprascapular regions. Pulse 130, temperature 99° at 3 p. m. daily. Cough worse at night, mucopurulent expectoration; repeated examination negative for tubercle bacilli. Urine pale straw color, acid reaction. Sp. Gr. 1009; no albumin, no sugar. I am indebted to Dr. George C. Johnston for the above clinical data, and agree with him in his diagnosis of this case, viz., general tuberculosis.

Examination. Ocular.—On inspection, the upper lid of each eye presents a well marked and pronounced swelling, with ptosis, entirely obliterating the infraorbital crease. The summit of this swelling is at the outer third of each superior lid and is slightly higher on the right side. On palpation the superior lids on light pressure feel soft and œdematous,

¹⁵ Loc. cit.

¹⁶ Tuberculose atténuée des glandes lacrymales; guérison spontanée. Ann. de la Société de médecine de Gand. 1896, lxxv, 105-119.

¹⁷ Vestnik oftalmol., Kiev., 1897, xiv.

the integument is freely movable and extremely lax. Firmer pressure reveals a tumor in each lid, hard, lobulated, rather firmly attached at its base and disappearing under the rim of the orbit. Each is joined to a flatter, equally hard, mass below (the enlarged accessory glands), more marked in the right lid.

The lids evert with difficulty and present a palpebral conjunctiva, red, rough, and thrown into folds, dotted with numerous yellow and yellowish-gray nodules. These nodules are in many instances broken down in ulceration. The lower lids are free from these nodules and ulcers although their conjunctiva is inflamed and rough.

The ocular conjunctiva, excepting a few enlarged vessels, is normal. Corneæ normal, with the exception of a slight diffuse haziness, seen only with oblique illumination. Drainage apparatus unaffected. Inspection of the nose and throat reveals nothing abnormal except a slight hypertrophic rhinitis, common in this locality.

A quantity of the discharge and curettings from the ulcers of the conjunctiva was collected, direct smears made on a slide and search made for tubercle bacilli, repeated every week, and always with a negative result. A portion of this matter was injected into the anterior chamber of a rabbit, with the result that in a few days the animal developed a severe iritis. The eye was enucleated in fourteen days, the iris examined for tubercular inflammation and tubercle bacilli, with negative results. A watery solution of the matter (about 3 cc.) was injected into the peritoneal cavity of a guinea-pig, followed in three days with violent local reaction from which the animal eventually recovered. Post-mortem and microscopical examination in four weeks revealed nothing tubercular, nor could a tubercular growth be cultivated at any time in the various media from the matter scraped from the lids.

The patient was given full doses of codliver oil and creosote, taken from school and made to live an out-of-door life as much as possible, with appropriate diet.

She was seen once or twice a week for a period of four months, during which time the enlarged lachrymal glands presented no change. The conjunctival ulceration improved under the home use of a 2 per cent protargol solution and application of a 2 per cent nitrate of silver solution at the clinic.

About the middle of January, 1901, the condition of the lachrymal glands was the same as when first seen, notwithstanding the fact that the other glands of the body which had been enlarged and tender, had become to all outward appearances normal. The conjunctivæ were still rough and presented many of the nodules as when first seen; the discharge and ulcerations were, however, markedly less.

The patient was lost sight of for about two months. Having received the advice to have the diseased lachrymal glands removed, with the fear and superstition characteristic of her race for any "cutting operation," she did not reappear in the clinic until the middle of March, when she presented herself much elated over the complete cure of her ocular malady.

On inspection the lids presented a normal appearance; their former fullness had entirely disappeared and it was only with the most careful palpation that a small, hard, scarcely perceptible gland could be felt by introducing the tip of the little finger well under the rim of the orbit. The everted upper lids showed a smooth glistening conjunctiva, entirely free from nodules and ulcerations and with but a slight degree of congestion. The general health of the patient has correspondingly improved; she has gained eighteen pounds in weight, is free from cough and night-sweats, and has a healthy, bright appearance. Some rough breathing can still be heard over the right apex, but no tubercle bacilli can be found in her much diminished expectoration.

The study of this and the twelve other reported cases appears to warrant the following conclusions being drawn:

1. Tuberculosis of the conjunctiva may be either ectogenous or entogenous; tuberculosis of the lachrymal gland must be hematogenous.

2. The presence of the tubercle bacillus in tuberculous conjunctivitis and tubercular dacryoadenitis is not a *sine qua non* of the disease. In the present case, repeated examination of the matter from the ulcers of the conjunctiva failed to show the presence of tubercle bacilli, nor did inoculation in animals produce the disease. Burnett¹⁸ speaks of a case he observed for more than a year, in which the clinical picture was one of tuberculosis of the conjunctiva, and yet he could not find a single tubercle bacillus after repeated examinations; inoculation in rabbits likewise proved negative.

3. Tubercular dacryoadenitis and conjunctivitis may undergo cure; surgical intervention is indicated only after therapeutic and proper hygienic measures fail, since it is a universally recognized fact that tuberculosis in other parts of the body is often cured outright spontaneously, the cure being effected by a marked increase of connective tissue.

NOTICE.

THE Committee on the Mütter Museum of the College of Physicians of Philadelphia announce that the Mütter lecture for the year 1901 will be delivered on Tuesday, December 3, at 8 P. M., in the Hall of the College of Physicians. Dr. Harvey Cushing, of Baltimore, will deliver the lecture, the subject being "Some Experimental Observations Relative to the Surgery of the Nervous System."

JOHN H. BRINTON,

GEORGE MCCLELLAN,

FREDERICK A. PACKARD,

Committee, Mütter Museum.

¹⁸ Diseases of the Conjunctiva and Sclera. System of Diseases of the Eye. Norris and Oliver. Vol. iii, p. 224.

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BULLETIN

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A CONTRIBUTION TO THE STUDY OF AMŒBIC DYSENTERY IN CHILDREN.*

BY SAMUEL AMBERG, M. D.,

Assistant in Pediatrics, Johns Hopkins University.

During fall 1900 and winter 1900-1901, 5 cases of amœbic dysentery came under observation at the children's department of the Johns Hopkins Dispensary, and were admitted to the hospital in Dr. Osler's service, whose kind permission enables me to report them. In his paper on amœbic dysentery Harris¹ comments upon the infrequency of the disease in children and young adults, the proportion being about 10 persons above, to 1 under 20 years of age. Of his series of 35 cases, 4 were under 10 years of age. There seem to be only two more cases on record, where amœbæ were found in children of the first decade of life in the U. S. Strong² encountered amœbæ in the tuberculous ulcers of the intestines of a 3-year old child, and Slaughter³ in a liver abscess of a boy 7 years of age. Of foreign authors Kurtulis⁴ states that dysentery befalls children of all ages with exception of infancy. Kurtulis does not expressly say amœbic dysentery, giving the division into the different types of dysentery in the subsequent pages, but amœbic dysentery is at least included in his statement. Pfeiffer⁵ found the amœbæ in the passages of several children. The child in whose passages Lambl⁶ discovered the amœbæ for the first time, was 2 years old, but the amœbæ found in his case were much smaller than those usually found in amœbic dysentery. Lutz⁷ mentions the occurrence of amœbæ in the passages of a little girl and Sonsino⁸ encountered them in the intestinal mucus of a child. Neither mentions the age of his patient.

Cahen⁹ reports a case of amœbic dysentery in a girl 4 years of age and Gneftos¹⁰ met the amœbæ in material of a liver abscess in a child 6 years of age.

In the following will be found short histories of our cases as they came under observation.

CASE 1.—Peter S., age 3 years, of Bohemian descent, came to the dispensary on Oct. 18, 1900, and was admitted to the hospital on Oct. 25th.

His complaints were pain in abdomen and bloody passages. During the summer he used to drink water from the gutter. His present illness began suddenly 2 months ago with frequent passages containing mucus and blood. The movements were associated with some pain. After suffering for 8 days with these symptoms he got a medicine lessening the frequency of the passage, but not the mucus or blood. There was no loss of appetite.

At the examination of the well nourished, rather pale boy heart and lungs did not present anything pathological. The abdomen was slightly distended, not tender on pressure. The edge of the liver was indistinctly felt, the spleen was not palpable. The movements of the bowels were accompanied by some pain. Patient was put to bed, received liquid diet and was started with irrigations of 400 ccm. of a 1:5000 solution of sulphate of quinine 2 times a day.

On November 1, patient was taken home not improved.

The frequency of his passages, not counting the irrigations, varied between 0 and 3. His temperature never exceeded 99.2°, mostly varying between 98° and 99°. After his dis-

* Read before the Johns Hopkins Medical Society, January 7, 1901.

charge the irrigations were kept up for a time at the dispensary, but the patient soon failed to appear.

On the 19th of February, 1901, the patient presented himself for the second admission.

The frequency of his passages had varied between 4 and 5 in 24 hours and sometimes he had lost a considerable amount of blood. The passages now contain pieces of blood-clots of about 3 cm. length.

The child was well nourished and not particularly anemic. At the physical examination nothing new was found. The treatment consisted in rest in bed, dieting, irrigations of quinine solution gradually increasing in strength from 1:5000 to 1:250 twice a day and bismuth subnitrate.

On April 6, the child left the hospital well.

The frequency of the passages never exceeded 5 in 24 hours. At the beginning of March the passages became more and more solid and formed, the amount of mucus lessened, and the blood disappeared. Since about a fortnight before discharge the discharge never contained any more mucus, blood or amœbæ. The temperature during the first week several times reached 100°; the highest temperature of 101° was noted on the 27th of February; it reached the normal line the next day, varying henceforth between 97.5° and 99°.

CASE 2.—John P., age 5 years, of Polish extraction, came to the dispensary on the 29th of October, 1900, and was admitted to the hospital on the 30th.

His complaints were loose bowels and prolapsus recti. Patient was born in Germany and came to this country 3 months ago. In September and October he spent 6 weeks in the country, near Aberdeen, the rest of the time he lived in Baltimore. The present illness developed while in the country. There is no history obtainable of drinking stagnant water. Patient was taken sick about 6 weeks ago after living for two weeks in the country. It came on rather suddenly with very frequent movements of the bowels, the passages frequently containing blood. The movements often were associated with severe straining. After a while the intestine began to come down with the passages, but again retracted shortly afterwards. Several times the child vomited. During the last few days the patient had chilly feelings and fever, but no definite chill. Appetite is poor.

The patient is a delicate, poorly nourished child. The visible mucous membranes are pale. The cervical glands are slightly enlarged. There is a slight œdema of feet and legs. The volume of the pulse is small, the rhythm regular. The tongue is clear. Percussion and auscultation of the lungs do not present any signs of disease. Over the whole heart a soft systolic murmur is to be heard, which is loudest over the apex. The abdomen is slightly distended and not tender on pressure. The liver is just felt, the spleen not palpable. The rectum prolapses with each passage about 4 cm. and is inflamed. Ulcers are not seen. The rectum retracts after some time. The passages are very painful.

Patient was put to bed, received liquid diet, and was started on quinine irrigations twice a day. The strength of

the solution was gradually increased from 1:5000 to 1:250 until the 21st of January, 1901, when the irrigations were stopped. From the 9th of December patient received as morning irrigation 500 ccm. of a 1:20,000 silver nitrate-solution instead of quinine. Of other medications he received bismuth subnitrate, which was changed later on to tannigen, and syrupus ferri iodidi.

The prolapsus of the rectum was not noticed after the second week in January. Towards middle of January patient acquired a good color, and felt very well. On the 26th of January he was discharged well.

During the first month patient had as many as 17 passages a day, but their frequency varied much; sometimes he had only 3. For a period of about two weeks before his discharge he had no more than 3 passages a day. After January 4, no more amœbæ were found. At the beginning of January the passages became formed.

Until the end of November the thermometer registered several times 100°, the highest temperature of not quite 101° being noted on the 18th of November. From the end of November the temperature can be considered as normal.

CASE 3.—William K., age 5 years, white, came to the dispensary on January 7, 1901, and was admitted to the hospital on January 8.

The patient's complaint was about a prolapsus recti. Several months ago, while picking strawberries in Anne Arundel County, the boy was taken sick with diarrhœa, having 5-8 loose passages a day, containing blood. At the same time his younger brother was affected in a similar way. Soon the bowels came down with every passage. The child never complained about pain or straining. The appetite was always good and he continued to play around.

In material taken with the rectal tube fairly numerous Chareot-Leyden crystals were found, but no amœbæ. The next day patient came back with his brother, in whose stool amœbæ were readily found, while the presence of amœbæ in the stool of the first patient was demonstrated only after admission to the hospital.

Upon examination, the boy seemed well nourished but a little pale. He had enlarged tonsils. On the 15th of January the patient was discharged, somewhat improved, to continue treatment at the dispensary. He was treated with irrigations of quinine. The mother brought him for a time regularly to the dispensary, but soon preferred to give him the irrigations at home. Up to the beginning of March patient did fairly well, having from 0 to 5 pasty movements a day. He was shown at longer intervals at the dispensary, where always motile amœbæ were found in his stools, with little blood and mucus. At the beginning of March he grew gradually worse. The bowels moved more frequently, the passages were loose, containing more blood and mucus. The prolapsus, which had disappeared, came back. Before his second admission on the 13th of March he had vomited twice. His appetite was poor. On the morning of his second admission the yellow liquid stool contained an enormous amount of amœbæ. Over the base of the left lung

the breathing had a tubular modification, and on inspiration fairly numerous medium moist râles were to be heard. The first heart sound over the apex was accompanied by a soft systolic murmur. At the base the heart sounds were clear. The abdomen was not tender on pressure; liver and spleen not palpable.

Patient was put to bed and placed on the usual treatment.

On the 21st of May he was taken home against advice, although motile amœbæ were found in his passages on day of discharge. The patient's general condition was much improved.

The frequency of the passages was 3 to 5 a day and their consistency became gradually firmer.

The temperature curve remained mostly around the normal line, the highest temperature of 100° was noted on the 4th of April.

CASE 4.—Michael K., age 2 years 8 months, white, came to the dispensary on the 8th of January, 1901, and was admitted to the hospital on the same day.

He complained about loose passages, containing blood. The disease was contracted at the same time his brother was taken sick, about May, 1900. Both were drinking pump-water. At first he had 2 or 3 loose movements a day, but their frequency increased gradually until now, the mother says, his bowels move nearly constantly. Blood in his passages was first noticed two weeks after onset. Patient did not suffer any pain and had always a good appetite. The child was fairly well nourished, pale, a little puffy about his eyes. The glands of neck, axilla and inguinal region were just felt, the epitrochlears were not. Phimosis. The tongue is slightly coated. The lungs are clear. Over the whole heart a blowing systolic murmur was heard, which was not transmitted into the axilla. The abdomen was a trifle full, not tender on pressure. Liver and spleen were not palpable.

He was ordered irrigations of quinine.

Patient was discharged on the 15th not improved, to continue treatment at the dispensary.

The number of passages varied between 1 and 4 a day; they were rather loose. The temperature curve reached not quite 100° on the first day and fell afterwards to the normal line.

Patient was brought for a short time to the dispensary, and afterwards received his irrigations at home. Until 21st of May he was brought at longer intervals. Then the family left for the country.

The frequency of his passages varied between 2 and 4. Sometimes they were more formed, at others loose. He never passed blood to a considerable amount. Motile amœbæ were seldom absent from his passages.

CASE 5.—Mary R., age 4 years, white, came to the dispensary on the 25th of February and was admitted to the hospital on the 26th.

The patient complained of diarrhœa, blood in passages and general weakness. The child was very fat before taken sick. The disease lasted about 5 months. Sometimes she had 5 to 6 movements a day. The passages sometimes con-

tained bright red blood. Child feels weak. Appetite was always good. Patient is a playmate of Peter S. (Case 1) and used to drink from the gutter too.

The girl appears to be well nourished and somewhat pale.

The examination of lungs, heart and abdomen did not reveal any pathological changes.

The child received the usual treatment and was discharged well on the 24th of March.

The number of the passages never exceeded 3. On some days she had no spontaneous passage. With the rather firm stools there came at first a little mucus and blood. From the middle of March no more amœbæ were found.

The highest temperature, 100° , was reached on the 28th of February. For the rest of the time the course remained just above the normal line.

On examination of the urine no albumen nor sugar was found in any of our cases, nor did it contain an extraordinary amount of indican.

At the end of August, 1901, we inquired into the state of health of our cases. John P. and Mary R. remained well. The father of William and Michael, who were still in the country, said the children did well and did not suffer any more from diarrhœa, nor were blood or mucus present in their passages. The statement must be taken with caution. Peter S. enjoyed very good health until the beginning of August, when he began to void blood after passing a formed stool. I could not prevail upon his parents to bring him to the hospital or dispensary.

The first factor of interest in our cases is their grouping. In two instances the disease befell members of the same family exposed to the same influences. Peter S. and Mary R. were playmates living in close neighborhood and drinking from the same contaminated sources. A third child of their company was taken sick with the same symptoms, and it is very probable that this child, too, had amœbic dysentery. Notwithstanding several efforts I was unable to obtain control over this last case.

The clinical type, to which our cases belong, is that of moderate intensity as described by Councilman and Lafleur.¹¹ Harris¹ gives a somewhat different clinical classification and places in his first group those of a very mild form, where the appetite and general health are good. Fever and acceleration of pulse do not exist worth mentioning. The number of stools varies from 2 to 6 in 24 hours. This, he states, is the usual form observed in children. With exception of John P. the type of our cases coincides very closely with this description. John P. must be classed in the second group, that of moderate severity, where the general nutrition is decidedly interfered with. The patient's general condition will best be illustrated by the blood-picture. There is frequently more or less anorexia, the pulse is somewhat increased in frequency and there are irregular exacerbations of temperature, particularly at night. The number of stools is from 8 to 15 in 24 hours. William K., before his second admission, seemed to be in a state of transition from the first group to the second.

A rather surprising feature in the clinical picture is the

little amount of discomfort, which the children of the first group experienced. None of the children, with exception of Peter S., and he not to any considerable extent, complained about any pain, even William K. was free from it, although he had a prolapsus recti. Mary R. complained only of a feeling of general weakness, which was not very pronounced at the time she came under observation. This circumstance makes it difficult to impress the parents with the necessity of putting the children to bed. Complete rest is a very important factor in the treatment, at least in regard to shortening the course of the disease. John P., a member of the second group, seemed to suffer severely at the time of his movements.

Of complications, we had in two instances a prolapsus recti, which was a little smaller and not as much inflamed in the case of William K. as compared with that of John P. In both cases the prolapsus was reduced spontaneously, the reduction in the latter case requiring more time.

In none of the cases was any sign of affection of the liver. Abscess of the liver, which is a rather frequent complication of amœbic dysentery in adults, seems to be of very rare occurrence in children. Unfortunately in the great majority of the cases of liver abscess in children, which are reported as following dysentery, there is no mention made of amœbæ, although, as Slaughter³ already mentions, in some of the cases we may suspect an amœbic origin. Oddo,¹² up to 1897, collected 12 cases of liver abscess following dysentery in children. From these cases there must be subtracted one case mentioned by Leblond,¹³ that of Easmon,¹⁴ who does not mention dysentery in the history of his patient. Furthermore, Hall¹⁵ reported his case as one of traumatic abscess of the liver. Neal,¹⁶ too, does not mention dysentery, but speaks of the presence of round worms in the intestines. There remain the following cases, first 3 cases mentioned by Leblond, those of (1) Miller (Transactions of Med. and Phys. Society, Bombay, 1848). (2) Menger, dysentery ancienne. The reference given I was unable to find. (3) Percira.¹⁷ He does not give the age of the child. Then follow the two cases of Legrand¹⁸ in children, 5 and 3 years of age, as No. 4 and 5. (6) Huybertz's¹⁸ case in a 6 year old boy. (7) Slaughter's² in a 7 year old boy. The cases of Chapple and Rosetti I was unable to find. Besides these cases we find one (8) reported by Johnston²⁰ in a 13 year old girl, and one (9) by Finizio²¹ in a boy 6 years of age, and one (10) by Gneftos¹⁰ in a 6 year old child. Including the first 3 cases of Leblond and those of Chapple and Rosetti, there are reported 12 cases of liver abscess in children following dysentery. Of all these cases motile amœbæ in material taken from the liver abscess were found only by Slaughter, while Gneftos reports the finding of dead amœbæ. The dysentery had persisted for a short time and no micro-organisms were grown from the abscess. In some of the other cases amœbic origin of the liver abscess is more or less probable. In the two amœbic cases the abscess followed the dysentery in a short time, as it seems to be the rule. Josserand²⁰ and Laferrère²¹ reported a series of cases, in which several years had elapsed between

the dysentery and the coming on of the liver abscess, and it remains to be seen, if this can happen in cases of amœbic dysentery too.

The reaction of the feces was mostly alkaline, seldom slightly acid. Sometimes in the acid stools the amœbæ continued to move for 2 to 3 hours. The microscopical appearance of the feces varied very much. In some instances they were rather firm and formed, carrying some bloody mucoid masses on the surface. Sometimes a formed stool was passed followed by blood either liquid or, rarely, in clots, accompanied by more or less mucus. In other instances the passages were semi-solid or uniformly liquid of different color with mucoid masses and blood intermingled. At times red blood corpuscles were only detected at the microscopical examination. The odor of the feces was always very offensive. In the cases of John P. and Peter S., and to a less degree in that of Mary R., there appeared towards recovery in the place of the mucoid masses stools of peculiar gelatinous consistence, which were found to be composed of continuous layers of epithelial cells.

The diagnosis was based upon the finding of motile amœbæ containing red blood corpuscles.

According to Harris'¹ method the surviving amœbæ were stained with toluidin blue in watery solution. A suitable piece of material is taken on a slide, a drop of the staining fluid is added and then a coverslip put on, or particles of the feces were put into the staining fluid and examined after a while. The endosarc is stained blue, while the ectosarc remains free or is stained later and less deeply. The only exception we have to make to Harris' statement is, that the amœbæ are by no means instantly killed by the toluidin blue. In some of the specimens motile amœbæ were found 3 to 4 hours after staining, even if the particles of feces had remained for about 1 hour or little longer in a rather concentrated solution of the dye. In a number of the amœbæ the endosarc was stained very appreciably and still they continued to move. As a whole, it seemed that the more intensely the endosarc was stained, the motility grew less, until at a certain period the motility ceases, which occurs in different phases of the movement, so that the amœbæ appear to be fixed in different shapes. Not in all instances did the degree of staining and the ceasing of the motility coincide, so that amœbæ with deeper stained endosarc continued to move, while less deeply stained ones appeared fixed. The vacuoles take the stain deeply and are hardly to be distinguished from the nucleus. In the lighter stained bodies the red blood-corpuscles are not stained; in deeper ones they are blue. The method is valuable only when applied to living amœbæ.

A very good effect may be obtained by staining the surviving amœbæ with methylene-blue and neutral red. Either of these may be applied in watery solution or in substance. The only difference between these two stains seems to be, that methylene-blue checks the motility of the amœbæ somewhat quicker than does the neutral red. As with toluidin-blue, the endosarc takes the stain, while the ectosarc remains

free. If a drop of a watery solution of neutral red is added on a slide to a particle of feces containing living amœbæ, there appear in the endosarc of those that are more distant from the stain, and while the surroundings remain unstained, a few round granules of different sizes stained red. The granules emerge and disappear with the movements of the amœbæ. Gradually more and more of granules take the stain, while nucleus and vacuoles still remain free. Then the margin of the nucleus seems to take the stain slightly, and then the vacuoles begin to stain. In this state the rest of the endosarc presents a more uniform and deeper staining. In the still deeper stained specimens the endosarc is still more uniformly stained, while nucleus and vacuoles do not stand out clearly any more and are hardly to be distinguished from each other. Under these circumstances the amœbæ have lost their motility; they are mostly round, but some are fixed in different phases of movement. The deep red endosarc is sharply defined from the white ectosarc. The picture is very striking. From the deeply red stained background the white endosarc stands out very clearly. In some of the specimens, perhaps dependent upon the reaction of the feces, the endosarc is more yellow. The loss of the motility seems to depend to a large extent upon the degree of staining. Some of the amœbæ, particularly when more diluted solutions are used, preserve their motility for hours.

The red blood corpuscles in the amœbæ remain for awhile unstained, then they become of a brassy color, at last red. The results obtained with methylene-blue are very similar. These methods of staining are only successful with living amœbæ. If the specimens are preserved, with the air excluded, they may keep for 24 hours. But, as a rule, the stain is not persistent and after the lapse of a few hours the specimens fade. Several attempts to preserve the specimens proved unsuccessful. Arnold,²² whose paper gave the suggestion of using neutral red and methylene-blue for our purposes, was equally unsuccessful in preserving his specimens.

Many of the authors writing about amœbic dysentery mention the occurrence of Charcot-Leyden crystals in the feces, Kruse and Pasquale²³ found the crystals in material taken from liver abscesses. Their presence in the feces of persons suffering with helminthiasis is well known. More interesting is their occurrence, where the intestines harbor parasites of a lower order. In our series the crystals were absent only in the case of Mary R. In the passages of the other children they were rarely absent, but their number varied very much. Lewy²⁵ emphasizes that a close relationship exists between these crystals and the eosinophile cells, although it does not appear that this relationship is always found (see Cohn,²⁵ Brown²⁸ and Schmidt and Strassburger,²⁷ these latter authors do not mention if in their examinations of the feces the eosinophile cells were numerous). Brown²⁸ and Ewing²⁹ mention that in several instances numerous eosinophile cells were found in the feces in company with the crystals. The only report of the occurrence of eosinophile cells, besides the crystals, in the passages of patients suffering with amœbic dysentery, is that of Roemer.³² In our

cases, with exception of Mary R., where only a few eosinophile cells were found, eosinophile cells and free eosinophile granules were never absent, but their number was subject to great variations. Sometimes a whole field contained hardly anything besides these cells and free granules. Some of the cells were mononuclear. The granules in the cells and outside were sometimes very large. The number of the cells was by no means always proportional to that of the crystals. As staining fluid, the eosinate of methylene-blue (the so-called Tenner stain, see Simon³⁰ and Ewing²⁹—addendum) proved very convenient. The crystals take a faint red color with this staining fluid, which, it may be mentioned here, does not offer any particular advantage for staining amœbæ. I did not succeed in adapting Lewy's method of demonstrating the association of the crystals with the eosinophile cells in tissues for the examination of the feces.

The picture of the feces was too inconstant to allow a conclusion in regard to a relationship between the numbers of amœbæ, crystals, and eosinophile cells. Nor was it possible to establish a distinct relationship between the number of crystals and eosinophile cells in the feces and the number of eosinophile cells in the blood, as will be seen later. Only in the case of Mary R. the small number of eosinophile cells and the absence of crystals coincide with an exceptionally small number of eosinophiles in the blood. In the case of John P. and Peter S., the crystals disappeared with the disappearance of the amœbæ and the eosinophile cells and free eosinophile granules became much less numerous. Monads were present in the stools of all the cases again, with exception of Mary R. They resembled pears in their shape with a flagellum at either end. They were not constantly found and when found their number varied much. The question arose, if there existed perhaps a relation between these elements and the crystals and eosinophile cells. The circumstances, that they were found rather inconstantly, the examinations of the passages of two adults suffering with amœbic dysentery, where crystals and eosinophile cells were numerous in absence of monads, and the notes of Roemer make it rather doubtful. Furthermore, in the diarrhœic passages of a child in the hospital an enormous amount of monads were present, while Dr. Boggs did not encounter the crystals at repeated examinations. Eosinophile cells were comparatively numerous.

It may be of interest to note, that the number of neutrophile elements in the passages, particularly well preserved ones was mostly very small and they seemed mostly to be less numerous than the eosinophile elements.

In specimens taken from the first passages of Peter S., a number of distinct nucleated red blood corpuscles was seen, and Dr. Fletcher noted in a fresh specimen obtained from Michael K., the occurrence of cells looking very much like nucleated red blood corpuscles. In both cases the blood did not contain normoblasts.

In regard to the presence of amœbæ in the feces of children suffering from other intestinal diseases, the negative experience of Cahen⁹ was repeated. On microscopical exam-

ination of at least a few hundred fresh specimens obtained from children suffering with intestinal disturbances during the last year, comprising the summer of 1900 and part of the summer of 1901, amœbæ were never encountered. Relatively few of the children were over 3 years of age. Although these examinations were for the greater part not made with the distinct purpose of watching for amœbæ, the large number of examinations, frequently including repeated examinations of the same individual, would not have given a negative result, if amœbæ were of frequent occurrence in intestinal diseases of early childhood, at least in this part of the country.

Monads were found in two instances, while only once a doubtful Ch. crystal was seen. Büeklers²¹ states that Ch. crystals were exceedingly seldom found in the passages of children, and only present in cases of helminthiasis.

A limited number of stools,¹⁷ containing more or less leucocytes and mostly red blood-corpuscles were examined in regard to eosinophile cells. In a few cases no eosinophiles were seen, in most of the cases, few or relatively few were present, while only in one case of a girl 1½ years old, few well preserved eosinophile cells, but a great amount of free eosinophile granules were present. Neutrophile elements were very rare. The ages of the children varied between 6 months and six years. Loos³⁵ mentions as a curiosity the presence of numerous eosinophile cells in the passages of a child suffering with follicular enteritis. In 16 of the 17 cases the neutrophile elements in the feces always exceeded in number the eosinophile elements. This was particularly evident in two cases with prolapsus recti.

The examination of the feces is to a certain degree unsatisfactory. At times little material is obtainable with the rectal tube, sometimes the passages contain but little suitable material, and if much suitable material is available, it is hardly possible to examine all and we must rely on samples. Thus a true picture of the contents of the intestines is not always obtainable.

In the case of Peter S., John P. and William K., Dr. Cole was kind enough to make the agglutination test with bacillus dysenteriae Shiga, and obtained a negative result with a dilution of 1:10. The bacteriological examination of the feces, in John P.'s case made by Dr. Cole, did not bring out any organism resembling the bacillus of Shiga. The method of examination followed the suggestion of Flexner.³⁶ From 15-20 plates, 25-30 cultures were taken in glucose agar and those not producing gas were followed out. With 2 different colonies of bacillus coli communis obtained from William K., and not producing gas, the corresponding agglutination test (1/10) was made with negative result.

Material taken from William K. was injected into the rectum of cats in two instances, with negative results. But these experiments were made under unfavorable conditions.

The examination was not made with the intention of entering upon the question of the etiology of the dysentery, since the newer investigations of Flexner³⁶ and particularly Strong³⁷—in whose papers the literature bearing upon this

question is thoroughly considered—confirm the views established by Kurtulis, Councilman and Lafleur, Kruse and Pasquale and others assigning to amœbic dysentery a place as a disease sui generis.

In the publications on amœbic dysentery little attention was paid to the examination of the blood. Councilman and Lafleur only speak of an anemia due to a deficiency in corpuscular elements and hemoglobin in about the same proportion. Lewis³⁸ found in a young man 17 years of age, sick 6 months, 4,000,000 red and 31,000 white blood-corpuscles, Preston and Ruräh³⁹ in a colored man, 22 years old, sick 2 months, 5,800,000 red and 5,600 white cells. Our specimens for the differential count were prepared after a method used by Dr. Ch. E. Simon for 18 months past. A drop of blood is placed on a clean slide and spread with the short, smooth edge of another slide, which is held at an angle to the first and drawn off without applying force. To obtain good results it is necessary that the whole procedure, from the moment the blood appears, takes as little time as possible. Ewing gives a similar method and describes the advantages of the method of taking smears on slides. As a staining medium the eosinate of methylene-blue proved satisfactory. (A table giving the result of the blood examination in each of the 5 cases will be found on the next page.)

In 4 of the cases there is a varying degree of anemia, which finds its expression more in a deficiency in hemoglobin, than in the red blood-corpuscles. In all the cases, there is a leucocytosis, in most of the counts not a very high one. Where the leucocytosis is more pronounced, the number of the polynuclear neutrophile element is increased. The subdivision of the lymphocytes into small and large ones was made on account of the striking appearance of the pronounced large forms, but the differentiation of the less pronounced forms from the small lymphocytes is frequently so difficult, that it is more or less arbitrary. From cells several times the size of an average red blood-corpuscle with a large, rather faintly stained nucleus and relatively little basophile protoplasm to the typical small lymphocyte all forms of transition are seen. A round nucleus does not belong to the characteristic qualities of these cells, as Geissler and Tapha⁴⁰ state. The fact that the nucleus may be karyoblastic (see Pappenheim⁴¹) makes their differentiation from other cells still more difficult. Frequently little vacuoles were seen in the protoplasm. The protoplasm looks sometimes rather uniform, in other instances it makes the impression of a coarse network and again it offers a more granular appearance. The amount of protoplasm is, as a rule, relatively small, but still somewhat greater than in small lymphocytes, sometimes it is considerable. To enter more closely upon this subject, this is not the place. In the first count only the pronounced cells are registered as large lymphocytes. In the subsequent counts the staining properties of the nucleus and the amount of protoplasm were taken into consideration besides the size. That these cells which were first counted separately by Einhorn,⁴¹

Date.	Hæmogl.	Red blood-corpuscles.	White blood-corpuscles.	No. of leucocytes counted.	Lymphocytes.	Large mononuc. + transition.	Polynuc. neutroph.	Eosinoph. leucoc.	Mast-Zellen.	Myelocytes.	Absolute eosinoph.	
1. Peter S. X. 22. 1900	60%	4,800,000	19,000	750	13.6 %	7.8 %	67.6 %	9.8 %	0.9 %	1862	
XI. 10.	1037	17.39 { small 14.86 % large 2.53 %	7.51	66.22	7.91	0.48		
XI. 12.	60%	4,800,000	20,000	1279	20.5 { small 10.33 large 10.17	9.66	62.11	7.27	0.86	1454	
II. 19. 1901	55%	3,900,000	15,500	1164	20.03 { small 4.03 large 16.00	9.87	60.6	9.28	0.51	1438	
IV. 1. Ward count.	60%	5,200,000	6,600	1359	20.9 { small 3.45 large 17.45	19.64	51.54	7.43	0.51	...	490	
X. 26. 1900	67%	4,480,000	17,000								
II. 22. 1901	68%	17,500								
2. John P. X. 31. 1901..	32%	2,200,000	18,000	1000	26.2 { small 23.4 large 2.8	11.0	59.5	1.9	0	1.4	342	12 normoblasts. 2 megaloblasts.
XI. 8.	1981	22.06 { small 16.14 large 5.59	11.46	59.52	2.77	0.15	4.19	9 normoblasts. 1 megaloblast.
XI. 18.	54%	3,600,000	12,000	1251	20.79 { small 14.08 large 6.71	12.78	62.34	4.11	0.32	0.39	493	No normoblast. No megaloblast.
XI. 30.	63%	4,000,000	10,500	1284	26.81 { small 15.67 large 11.14	17.21	51.59	4.05	0.46	1	425	No normoblast. No megaloblast.
XII. 2. Ward count.	55%	4,200,000	11,500	1486	26.2 { small 12.39 large 13.81	13.12	58.72	2.22	0.4	0.2	255	1 normoblast.
XI. 11. 1900	11,000	548	14.66	19.04	61.15	2.56	2.19	281	
I. 23. 1901	63%	4,940,000	8,600	306	24.0	20.0	52.3	3.00	258	
3. William K. I, 11, 1901	50%	5,000,000	13,800	1557	26.84 { small 9.25 large 17.59	12.01	57.8	3.01	0.51	415	
II. 21.	40%	5,000,000	14,000	2864	21.24 { small 6.32 large 14.92	5.58	71.42	1.81	0.06	253	For this difference no reason could be found.
V. 2. Ward count.	85%	5,000,000	14,000	1397	28.96 { small 2.07 large 26.89	15.29	50.25	5.08	0.85	711	
III. 20.	51%	6,500,000	17,500									
4. Michael K I. 9.01.	50%	4,500,000	27,000	1394	19.0 { small 7.96 large 11.04	9.18	69.44	2.65	0.14	715	
III. 9. Ward count.	40%	4,500,000	17,000	1596	29.58 { small 6.7 large 22.88	8.01	47.61	13.73	0	2334	
I. 9.	45%	4,500,000	27,600									
5. Mary R. III. 1.01.	68%	5,400,000	24,300	1243	10.34 { small 0.48 large 9.86	8.36	80.64	0.16	0.4	38	
Ward count.												
II. 21.	70%	17,740									

are frequently found in the blood of children is well known, and that the typical small lymphocytes are sometimes rare is mentioned particularly by Hoek and Sehlesinger.⁴³

In regard to the number of eosinophile cells in the blood of healthy children the figures of the different authors vary much. Hoek and Sehlesinger find a variation from a few hundred to several thousand in a cmm. during childhood. The figures of Gundobin⁴⁴ and Weiss⁴⁵ are based upon examinations of younger children. Canon,⁴⁶ Fisehl⁴⁷ and Carstanjen⁴⁸ do not give the actual leucocyte count, and so these figures are not of much value to decide, if there exists an eosinophilia or not. The average percentage of the eosinophiles as given by Carstanjen for children from 2-3, 3-4, 4-5 and 5-6 years are 3.9%, 5.74%, 6.3%, and 6.22%, the last three the highest average figures during childhood. The maximum figures for these periods are 6.2%, 9.95%, 16.65% and 9.1%. Lappert's figures for 2 normal boys 5 years of age are 3.97% and 8.8%, the absolute figures being 361 and 660 in the cmm.

Our cases William K. and Michael K., who left the observation without being cured, seem to show a tendency to in-

crease their relative and absolute eosinophiles. Mary R. takes here too an exceptional standpoint in our series. The figures of John P. show a slight decrease towards recovery, while in the case of Peter S. a marked diminution of the absolute number of the eosinophiles is shown. In this instance we may be permitted to interpret the higher figures prevailing during the disease as a slight degree of eosinophilia associated with the disease [the anemia may have exercised an influence upon the first figures].

The initial blood-picture of John P. very clearly demonstrates the poor condition of the patient's general health. In the first two examinations the red blood-corpuscles varied very much in size, there was a slight poikilocytosis; a few pronounced megalocytes and microcytes were present. Many of the red blood-corpuscles were polychromatophilic, but granular degeneration was never found. With the increase in hemoglobin and in the red blood-corpuscles the blood-picture came nearer and nearer to the normal. The number of blood-platelets seemed slightly increased at first, certainly they were somewhat less numerous later on. As myelocytes were counted all the mononuclear neutrophile elements.

But particularly in the second count quite a number of these cells did not exceed in size the usual polynuclear neutrophile leucocytes. The nucleus was more centrally located, and it resembled more that of the polynuclear neutrophile leucocytes in its staining properties. All these characteristics suggest that these cells do not belong to the typical myelocytes of Ehrlich, and it would, perhaps be better to follow the example of Tuerk⁵⁰ and to designate these as mononuclear neutrophile leucocytes. The frequency of these cells decreased rapidly, and on subsequent examinations they were only occasionally found. In the first specimens a very large neutrophile leucocyte was seen, whose nucleus was divided into four distinct, faintly stained parts. The body of the leucocyte was connected by a small bridge with a small globule apparently in the process of separation from the large cell. The whole was filled with neutrophile granules. At subsequent examinations of specimens of the same date one more cell of this kind was found, but without the globule. Besides this form, one cell was seen resembling the small neutrophile pseudolymphocyte of Ehrlich, that is a small mononuclear neutrophile cell. The only difference was that the nucleus did not take the stain very deeply, while the nucleus of Ehrlich's form requires a great affinity for basic dyes. The difference may be due to the different method of staining. Ehrlich⁵¹ found these forms in hemorrhagic small-pox and in fresh pleuritic exudates. Relatively frequently a form was seen about $1\frac{1}{2}$ to 2 times the size of a typical small lymphocyte, seldom larger, where the nucleus could hardly or not at all be distinguished from the protoplasm. The whole was more or less deeply stained and looked like a deranged, rather coarse network.

The small number of red blood-corpuscles at admission, the corresponding low percentage of hemaglobin, the poikilocytosis and polychromatophilia, the presence of normoblasts, megalocytes, megaloblasts and myelocytes indicate a rather severe secondary anemia. The presence of myelocytes in anemic conditions of children is not unusual, and Cabot,⁵² who gives a short review of the cases, where they were found in adults, comes to the conclusion, that their appearance has perhaps the same significance, as the appearance of normoblasts.

The case of John P. may give rise to the suggestion that the blood picture may assist to complete the clinical classification of amœbic dysentery. In his case at least it falls in very well with the other clinical picture.

The loss of blood does not seem to have been the only factor in bringing about the anemia. Even if we consider the frequent passages, he never lost as much blood as Peter S. The hygienic surroundings of John P. did not differ materially from that of the other children.

The number of our blood examinations is not sufficient to allow definite conclusions. In one case, that of Mary R., an exceptionally low number of eosinophile cells in the blood corresponds with the absence of Charcot-Leyden crystals and with a small number of eosinophiles in the feces. This would correspond with Bücklers' experience in helminthias-

is. In our series we can hardly say that strikingly high percentage of eosinophiles is associated with the presence of numerous crystals. But it may be that our cases correspond with those of Bücklers where a slight eosinophilia was found by presence of many crystals, and subsequent examinations may show that amœbic dysentery does not differ materially, in regard to the crystals and eosinophile elements, from helminthiasis. The only one of our cases which shows a distinct, if slight, eosinophilia is that of Peter S., while the figures of Michael K. are at least suggestive.

One circumstance certainly deserves attention. If in the passages of a child—at least in this part of the country—Charcot-Leyden crystals are found, we have to take into consideration the possibility of amœbic dysentery, a fact which it will be well to remember, since the amœbæ themselves may only be found after repeated examinations. What the significance of the eosinophile cells is remains to be seen. Their numerical relation to the neutrophile elements may perhaps be of some value.

I will add a short history of another case, which could not be fully considered, because the patient did not come under treatment.

Katie N., 8 years of age, white, living in Baltimore, came to the dispensary on September 9, 1901. She complained of chills and fever and diarrhœa. She has had diarrhœa for a long time, passing mucus and sometimes blood with much pain and tenesmus. Besides she has much pain in lower abdomen. Present illness began 5 days ago with shaking chills followed by fever, in which she is delirious. She has had a chill every day since at about the same time. No more bleeding. The child was rather pale and thin. Heart and lungs were clear. The spleen is enlarged and the abdomen is rather tender on pressure. Rose-spots. Temperature 100.4° . No plasmodia malariae were found in the blood. The feces (rectal tube) looked very typhoidal. At the microscopical examination no Charcot-Leyden crystals and no monads were seen; there were very few cellular elements. In nearly every specimen one or more motile amœbæ were found, but none of them contained red blood corpuscles.

It is very probable that in this case a typhoid fever (?) superposed itself upon an existing amœbic dysentery, but the examination is not sufficient to make a definite diagnosis.

NOTE.—While this paper was in print a white boy, 2 years 8 months of age, of Polish descent, was brought to the dispensary suffering with loss of appetite, vomiting and very frequent bloody passages associated with pain. The people live in the southeastern part of the city. The present illness has lasted 12 days. The boy was very weak, the pulse quick and small, the temperature 100.8° . The rectal tube brought a small amount of bloody mucoid material with a very offensive odor. Numerous motile amœbæ containing red blood-corpuscles were seen under the microscope. A few monads were present and bismuthsulphide crystals, but no Charcot-Leyden. His death prevented further examinations. An autopsy was not permitted.

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THE ADVANCES MADE IN MEDICAL AND SURGICAL DIAGNOSIS BY THE RÖNTGEN METHOD.¹

BY CHARLES LESTER LEONARD, A. M., M. D., of Philadelphia.

The Röntgen method of diagnosis is the result of an evolution which followed the discovery of a new form of physical energy, possessing the peculiar property of penetrating and producing shadow pictures of the otherwise invisible portions of the body.

The development of this method of picture making, into a method of physical diagnosis, was necessary to its employment in medicine and surgery. It was necessary to apply accurately, with precise methods, its power to obtain mechanically data upon which a diagnosis can be based.

Like all other diagnoses a Röntgen diagnosis must be based upon normal and pathological anatomy combined with X-ray technique and clinical experience. A medical education is therefore a prerequisite to its accurate application in diagnosis.

The observer must possess the knowledge of what to look for, as well as how to look, and in addition he must be able to interpret what he sees. The Röntgen diagnostician must acquire by clinical experience the ability to obtain and interpret correctly the data upon which he bases his diagnosis. This is the personal element in this otherwise mechanical method. It can be eliminated to a great extent, since the data are mechanically registered and hence can be studied by different observers and compared with the normal and pathological findings in similar cases.

The futility of attempting to utilize the data obtained by this method without accurate knowledge of the exact process by which they were obtained has often been demonstrated. Such attempts have led many surgeons into errors, and go a long way toward making up the sum of those cases in which this method of diagnosis has been said to be at fault. Undoubtedly the most experienced may err, but the errors are

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not due to the *means* employed to make the diagnosis, they are the result of *improper use* in the methods of employing it, and of erroneous interpretations. Clinical experience has demonstrated the accuracy of this method when correctly employed. The mechanical element in this diagnosis assures its accuracy. Data can be obtained that can be compared with mechanically recorded normals. It is this element that gives the clinical thermometer its value. It has determined the normal temperature and its physiological variations, and measures mechanically pathological variations from that standard. Even this simple instrument in diagnosis must be employed and read correctly.

In a technique capable of employing this method in physical diagnosis, is included a knowledge of the varying qualities of the Röntgen ray, and of the method of employing in each case the particular quality required to secure the desired data. This variation is necessary for different purposes and for the examination of different parts of the same individual. In the more difficult diagnoses, where more delicate differentiations are required, the quality of Röntgen discharge must be adapted to the individual case.

In many cases this method of diagnosis should be employed primarily, as in locating foreign bodies and in the diagnosis of fractures. Here the results are more accurate and comprehensive than can be obtained by other methods, while the dangers from infection, additional trauma, and devitalization of tissue are avoided. In other cases the best results can be obtained by employing this method to differentiate secondarily between possible diagnoses. Again, its only use may be to confirm, in a measure, a previously formed diagnosis.

The Röntgen method of diagnosis has as yet limitations in its application. In certain directions an absolute positive or negative diagnosis can be rendered. In others it aids. While it is as yet absolutely without value in other cases where its future development may render it of the first importance.

I shall touch upon only a few fields in diagnosis where the advance made is most clearly illustrated.

Although the advance in the diagnosis of fractures has been very marked, and of the utmost value in directing treatment, there are few surgeons who have fully realized, appreciated, and used this method to its full extent. One of the principal advantages of this method is that without producing pain it secures more absolute and accurate knowledge than the older methods, and does not produce any further trauma or endanger neighboring structures. Pain is nature's signal of injury to tissue. The anæsthetic hides it, yet the injury inflicted during manipulations and examinations must be considerable. The reparative process is delayed in proportion to the amount of trauma inflicted. The production of preternatural mobility and crepitus must frequently destroy connecting bands of periosteum, produce fragments, and increase oozing. Our knowledge of reparative processes teaches, that these elements are detrimental to rapid union and that they must be absorbed before union can take place. In im-

pacted fractures a diagnosis established in any other way seriously increases the severity of the injury.

The accuracy and detail which this method furnishes are of great value in directing treatment. An undetected comminution delays repair and frequently results in non-union. The callus thrown out from a linear fracture that enters a joint, or an undetected interscapular fracture will injure the functions of the joint unless the proper course of treatment is pursued. The shape and position of the line of fracture direct attention to the difficulties and complications that may attend the treatment, and help in avoiding them. This knowledge also aids in reducing the fragments and securing exact coaptation. The success of attempts at reduction and the value of the fixation apparatus are readily determined. The accompanying illustrations point out the value of this method in detecting rare fractures, and illustrate its accuracy in determining the presence of interscapular fractures that would otherwise escape detection.

The treatment of fractures by open operation is a well established practice and a marked advance. The Röntgen method of diagnosis forms the basis for the division of fractures into those that demand operation and those that can be properly reduced and treated by the older methods. Where the skiagraph shows that proper reduction cannot be secured or that the fragments cannot be maintained in correct apposition by ordinary fixation apparatus, the patient should have the facts, including the skiagraph, fully explained to him, and should be given his choice between imperfect union and operation.

The accuracy which has been attained by this method of diagnosis is such, that, although there are still certain portions of the skeleton where fractures cannot be excluded, yet, where a skiagraph can be obtained, having sufficient definition to justify a negative diagnosis, the patient should *not* be treated as if he had a fracture. All fractures of the limbs can now be readily excluded. Before the development of this accurate method it was good surgery to treat suspected fractures as if a fracture existed. To-day, such a course can only be justified by the inability to have a Röntgen examination made.

The exact determination of congenital osseous malformations and defects by this method of examination has aided materially in establishing diagnoses before orthopædic operations, and helped the operator to plan the intervention before the actual operation is undertaken. It has done much in differentiating between the various forms of congenital dislocations and malformations of the hip joints, a condition which one of the accompanying skiagraphs illustrates.

The application of the Röntgen method to the diagnosis of renal and ureteral calculi has supplied a deficiency in surgical diagnosis. The kidneys are anatomically situated in a position of the greatest safety. They are, however, for that reason, difficult to reach by ordinary methods of physical diagnosis. They are also surrounded by other viscera whose pathological lesions present a symptom-complex that it is often impossible to differentiate from renal disease except by



FIG. 1.—Normal foot.



FIG. 2.—Diastasis of periosteal scale at the attachment of the tendo Achillis, the result of muscular strain.



FIG. 3.—Fracture of internal malleolus.



FIG. 4.—Ankylosis of knee, resulting from rheumatoid arthritis.



FIG. 5.—Separation of symphysis pubis.



FIG. 6.—Congenital dislocation of both hips.



FIG. 7.—Calculi in left and right kidneys.



FIG. 8.—Multiple renal and ureteral calculi.



FIG. 9.—Ureteral calculus, just above sacrum.



FIG. 10.—Phleboliths in veins of broad ligaments.

exploratory operation. When, however, the diagnosis has been reduced to one of peri- or intra-nephritic conditions the problem still remains a very difficult one.

This method has therefore many advantages, since it is possible by its use to absolutely exclude or detect all calculi. Other renal conditions justify exploratory operations, but no other condition justifies incision into an apparently healthy kidney. Where calculi have been excluded by this method, incision into the kidney during an exploratory operation can only be justified by the presence of macroscopic pathological conditions.

Double exploratory nephrotomy has been suggested as a method of determining the presence of calculi in the second kidney where the destruction of one kidney by an abscess, the result of calculous nephritis, demands a nephrectomy. By this method the presence of calculi in both kidneys can be determined before operation and the proper procedure decided upon. The exclusion of calculi from the kidneys and ureters removes this source of danger as a complication of any operative intervention that may be necessary upon the other kidney or ureter.

Early operation in cases of calculous nephritis and ureteritis is of great importance. Statistics show that the gravity of any operative procedure increases with the length of time the calculus has been in the kidney, but more especially by the presence of infection. A calculus in a kidney invites infection. Early detection and removal are therefore very advantageous.

There are, however, graver reasons than these for early diagnosis and removal. These small calculi are not only a menace to the structure of the kidney, but also to its function. Those that produce the fewest symptoms often give rise to the most serious condition. Calculous anuria from the impaction of one of these small calculi in the ureter and its occlusion, menaces the life of the patient as well as the integrity of the kidney involved. If the other kidney is unable to carry on the function for both, it often ceases to act, a complete anuria follows and the patient dies. The other kidney may already be the seat of calculous disease, or its ureter may have been occluded at some former time and its function destroyed.

These are the dangers that threaten the patient who has an unsuspected or an undetected calculus. The Röntgen method detects suspected calculi and permits early operation. It changes a condition of indefinite danger into a condition that is safe and amenable to immediate operation if it is

necessary. It makes the non-operative treatment of cases suspected of calculus rational, because the position of the calculus is known or all calculi are excluded.

It has made an expectant non-operative treatment rational in certain cases where calculi are found in the pelvic ureters, and the symptoms point to recent progression down the ureter and the preservation of full renal function. In cases of complete anuria it directs operation immediately to the calculus, if that be its cause. The information secured by this method is very comprehensive and renders every operation complete. It limits operation to the exact seat of the calculi. It is no longer necessary to open and explore the hydronephrotic kidney to find as its cause a calculus in the pelvic portion of the ureter. The operation is limited to the removal of the calculus. The exact as well as the general position of calculi and their number are shown in the skiagraph.

Thus a calculus in one pole or calyx of the kidney can be removed through a small incision without the necessity for further exploration. Operation based upon the Röntgen diagnosis must be complete, as the number of calculi are known and their presence or absence in the other kidney or ureter has been ascertained.

This summary of the advance made by the Röntgen method of diagnosis in the detection of renal and ureteral calculi and their exclusion, is based upon the examination of 163 suspected cases and the detection of calculi in 47.

A further proof of the actual advance, is the need for the revision in our ideas of the relative frequency of renal and ureteral calculi. Renal calculi have been supposed to occur the most frequently. The results of this method of examination show that of 47 cases in which calculi were detected, in 27 the calculi were found in the ureter.

The minuteness of the calculi that can be detected is shown by the passage of calculi in five cases in which each weighed less than one grain. The minute detail obtainable is rendered evident by the detection recently of phleboliths, which in a measure complicated the diagnosis. In one case a calculus was found, which examination showed was a phlebolith in the vaginal wall. In a second case six phleboliths were found in the venous plexus of the broad ligament, as was demonstrated by a subsequent coeliotomy.

NOTE.—As much of the detail is lost in the process of reproduction the positions of the calculi have been designated by dots.

THE JOHNS HOPKINS HOSPITAL BULLETIN.

The Hospital Bulletin contains details of hospital and dispensary practice, abstracts of papers read, and other proceedings of the Medical Society of the Hospital, reports of lectures, and other matters of general interest in connection with the work of the Hospital. It is issued monthly.

Volume XII closes with this number. The subscription price is \$1.00 per year. The set of twelve volumes will be sold for \$23.00.

PATHOLOGICAL REPORT UPON A FATAL CASE OF ENTERITIS WITH ANEMIA CAUSED BY *UNCINARIA DUODENALIS*.¹

BY JOHN L. YATES, M. D.,

Assistant in Pathology, Johns Hopkins University.

The case here reported is the first published occurrence of the disease in Maryland. During this year eight unmistakable cases have been reported in this country, a number equal to all of those heretofore on record where the diagnosis is indisputable.

That many individuals harboring *Uncinaria duodenalis* have not had their affection diagnosed there is no doubt, and its prevalence in this country is certainly greater than has been supposed. Being endemic, as it is in Porto Rico and the Philippines, the importance of an early recognition will be even greater.

The appended list of cases reported from the United States shows that the disease is not localized in the South and demonstrates how easily contamination may be spread, five of the sixteen positive cases having contracted the disease in this country.

The patient who is the subject of this report was admitted to the medical department of the Bay View Asylum, October 2, 1901, and came under the care of Dr. R. Lee Hall,² to whom I am indebted for notes on the clinical history and for the privilege of examining the dried-blood preparations which he made upon two occasions. The history of the case is as follows:

J. O'R., English sailor, aged 39 years.

The past history developed nothing of importance. It was not clear where the disease had been contracted. His only known stop at a tropical port (Vera Cruz, Mexico), was immediately before his arrival in Baltimore and after the onset of his symptoms.

He had been feeling badly for six months, his appetite and digestion were poor, and colicky abdominal pains were present with some diarrhea. No cough nor night sweats were noticed, but there had been some dyspnea. About four weeks before his admission he had become decidedly worse. There had been a noticeable loss in weight, the diarrhea and abdominal pains had increased and blood had appeared in the stools. The dyspnea increased.

At the time of entrance to the Asylum nothing of importance was revealed by physical examination aside from a rather pronounced anemia with poor general condition and a noticeably dulled mentality. The area of cardiac dullness was not increased, an inconstant hemic murmur was noted at

the apex. There were some points of localized abdominal tenderness. The specific gravity of the urine was 1010; no albumin nor casts were present.

On the 9th day after admission a blood count made by Dr. Hall showed the following conditions:

Red blood-corpuscles	2,500,000
White " "	24,000
Hemoglobin was not estimated.	
Eosinophiles ³ about	25%
No normoblasts were seen.	

The anemia became more and more profound, and on the 17th day another blood count showed:

Red blood-corpuscles	800,000 (16%)
White " "	29,600
Hemoglobin	11%
Eosinophiles about	3%
Normoblasts were present but not abundant	0.8%

The patient's general condition grew gradually but progressively worse from the time of his admission. There was no extensive hemorrhage from the bowels. The stools were fairly frequent and tarry in character. Abdominal pains persisted.

On the 18th day he had become very much worse, the respiration and pulse gradually grew weaker and he died quietly at 7.30 P. M. At a necropsy done 18 hours later the following conditions were found:

Body.—The body, 173 cm. long, was emaciated and very pale, the skin had a peculiar yellowish tint. The conjunctivæ and mucous membranes were extremely anemic. Slight rigor mortis was present. The peritoneal cavity contained no excess of fluid, the serous surfaces were smooth and free from adhesions. The upper portion of small intestines was moderately contracted and somewhat whitish. In the cecum and large intestine, which were rather distended and very translucent, were scattered black foci that suggested ecchymotic patches in the intestinal wall, but proved to be bits of fecal matter adherent to the mucous surface.

Thorax.—The pleural cavities contained pale, slightly turbid fluid in moderate amount. There were a few adhesions on the right side. On the left side very soft, white and edematous adhesions were general except along the posterior aspect.

Pericardial cavity contained a small amount of similar fluid. Both serous surfaces were smooth and shiny.

¹Stiles: Texas Medical News, July, 1901, p. 523. The priority of *Uncinaria* to *Anchylostoma* as the name of the genus is pointed out and its employment therefore positively indicated.

²Dr. Hall has made a clinical report of the case which was published in The Journal of the American Medical Association, November 30, 1900, p. 1464.

³The differential counts were little more than approximate as the specimens stained poorly. The eosinophiles were, however, easily recognized and that proportion is fairly accurate.

Heart was very slightly enlarged, weighing 370 grammes. The contained blood was very pale and watery. The two sides were partially filled with a continuous tenacious clot, colorless and translucent. The valves were apparently normal. The myocardium, which was very pale and soft, contained a few opaque areas. The aorta showed but very slight changes.

Lungs.—Both lungs were voluminous and everywhere crepitant. The left lung was covered with the hairy white adhesions above described. Both showed on cut section considerable pigmentation and very pronounced pallor with a greatly increased juiciness of the dependent portions, particularly on the left side. The bronchi, filled with pinkish frothy material, were not injected.

Spleen.—The capsule was wrinkled, pulp was very soft, pale and friable. The Malpighian bodies were easily recognized. The organ weighed 100 grammes.

The liver was not enlarged. Surface was smooth and on it were very striking, white bloodless lines, appearing like intestinal lymphatics filled with chyle. The cut surface was of a light yellowish-brown color. The lobules were not definitely made out. The weight was 1350 grammes.

Kidneys.—The capsules were very slightly adherent; stellate veins not injected. The cut section showed the cortex to be somewhat cloudy and the cortical striæ were not recognized; the glomeruli were visible.

Bladder was distended with pale, clear urine; the mucosa was perfectly smooth and dead white in color.

Stomach contained much tenacious mucus mixed with coffee-ground-like material. The mucosa was very pale.

Duodenum.—Passing downward, at a point corresponding to the 3d portion, hemorrhagic contents were first encountered, and in this material a few adult *uncinaria* were found.

Jejunum and Ileum.—The mucoid nature of the contents persisted from the stomach to the cecum, but this material was blood-stained throughout. The mucosa was everywhere pale, the more prominent portions like the edges of the valvulæ conniventes were slightly injected. No ulcerations were noticed.

The worms, which were present in large numbers (probably thousands), were in a living condition and many were found with their head ends buried in the mucosa. These were quite firmly attached and were only separated with some force; there was left behind a sharp punched-out hole similar to a pin prick, with a reddish base and a slightly raised margin. No surrounding halo of injection was recognized. The amount of the muco-hemorrhagic material was greatest where the worms were most numerous. The process was apparently more advanced in the lower jejunum and in the ileum than in the duodenum. No parasites were observed in the last few centimeters of the ileum and at the ileo-cecal valve the contents changed in character.

Large intestine was filled with seybulous tarry feces and no parasites were observed. No ulceration was noted, though the rectum and sigmoid flexure were somewhat injected.

Brain was extremely anemic in appearance, but was otherwise apparently normal.

A detailed description of the parasites and ova will not be given. There was no difficulty in their identification, as the conditions found agreed absolutely with the accepted descriptions of the parasites. The female nematoid worms were 8 to 10 mm. long and showed at one extremity a buccal cavity armed with hooklets. The other extremity was conical. They contained ova and red blood-corpuscles. The male parasites, which were decidedly smaller (0.5 cm. long) also contained red blood-corpuscles, and at the tail end had the expanded bursa copulatrix.

The ova, which were ovoid in shape, contained a granular central portion surrounded by a narrow capsule of clear translucent material. No attempt was made to estimate the probable number of parasites present nor the relative frequency of the sexes, though it appeared that the females exceeded the males by a greater ratio than that usually mentioned (4 to 1). All the females examined contained ova, and these ova were found in the greatest profusion in the large and small bowel. Specimens of the intestinal contents also contained a great many Charcot-Leyden crystals.

In certain of the ova from the intestine segmentation had begun. By keeping some of the intestinal contents moistened and at a moderate temperature (about 28° to 29° C.) development of the ova into rhabditiform embryos was observed.

Microscopic Examination of Tissues.

Lungs showed considerable coal pigmentation and edema.

Spleen.—The Malpighian bodies are small in proportion to the pulp. The striking peculiarity of the latter was the presence of eosinophiles in great number, as many as a dozen often appearing in one field of the oil-immersion lens (Zeiss, ocul. No. 1, object. 1/12). They were slightly larger than the polymorphonuclear leucocytes and the nucleus was rarely round or horseshoe-shaped, but more often was bilobed or trilobed. The nucleus usually had a vesicular appearance, but in a much smaller proportion stained deeply and homogeneously. No evidence of nuclear segmentation was recognized. No nucleated red blood-corpuscles were seen.

Liver.—The changes in the liver were very widespread and striking. In the specimen examined each lobule contained an area of necrosis, invariably located about the central vein. The size of these foci varied from a few cells about the vein in some instances to an extent involving one-third or even half the distance to the periphery of the lobule in others. The outline of the necrotic areas was irregular but fairly sharp. In them the nuclei of the liver cells remained unstained and the protoplasm stained deeply in eosin. The transition from the living liver cells was quite sudden, karyolysis rather than karyorrhexis having occurred. Red blood-corpuscles were frequent about the necrotic cells and, unlike those in the capillaries elsewhere, stained deeply with eosin. There was also a limited infiltration with polymorphonuclear leucocytes and the endothelial cells of the capillaries had apparently undergone some proliferation. The wall of the central vein had a hyaline appearance but the nuclei of the intima were recognizable. In the necrotic areas, especially in the smaller less

advanced foci, were frequent deposits of a bright yellow pigment which was refractile and granular. This occurred in and about the cells and was not observed in the peripheral portion of the lobule where the cells were well preserved. The condition presented in the liver was the form of central necrosis described by Mallory (1).

Kidneys.—Scattered in the cortex, usually below the capsule, were a few small foci showing an increase in connective tissue with destruction of renal elements, the glomeruli undergoing hyaline degeneration, and a few of the tubules being atrophic and containing hyaline casts. The epithelial cells were very granular in appearance.

Intestine.—The intestinal contents were made up of altered blood, mucus, bits of mucosa, cells which are more or less degenerated and numerous ova, Charcot-Leyden crystals and swarms of microorganisms. Here and there were sections of the parasites, but in no place was the cephalic extremity found in close relationship to the mucosa.

In some specimens the mucosa was everywhere partially, and in some foci completely, necrotic in appearance. Not an intact villus was found, and even the glands of Lieberkühn were not completely preserved. It was difficult to make out the extent of the ante-mortem destruction of the mucosa. In other instances the preservation of the tissue was such that but slight ante-mortem destruction seemed probable. The basal part of the mucosa was infiltrated with eosinophiles in enormous numbers, so closely packed together that seventy-five were counted in one field of the oil-immersion. They were essentially of the type described in the spleen and appeared to have replaced the lymphoid elements which are normally present in such large numbers. There was an induration of the tissue with fibroblastic cells. In the submucosa eosinophiles were present in almost equally great numbers, occurring packed together in groups and rows between the fibrous tissue strands. Eosinophilic cells were found in small numbers within the interstitial tissue of the circular muscular coat but less frequently in the longitudinal coat. A few were present beneath the serosa. They were also seen to have penetrated the glandular structures and were found between the epithelial cells and in the lumina of the glands. No eosinophilic cells were found with signs of nuclear division. The nuclei of certain of these eosinophiles were seen to stain deeply and homogeneously, the eosinophilic granules becoming somewhat pale and less distinct. The nuclei in this instance took on a much more polymorphous form, finally undergoing fragmentation into numerous small particles. In a few cells with fragmented nuclei the granules were still to be recognized, where as a rule only a faint pink homogeneous cell-body was visible. Since this fragmentation was most marked nearer to the mucosa and in the points of greatest infiltration and was present to a comparatively slight extent in the spleen it was probably the result of a degeneration caused by the action of some toxic substance.

Anatomical diagnosis.—Catarrhal gastro-enteritis with hemorrhage caused by *Uncinaria duodenalis*, anemia, effusion

in pleural and pericardial cavities, edema of the lungs, fibrinous pleurisy, dilatation and hypertrophy of the heart (slight), central necrosis of the liver, chronic interstitial nephritis (slight).

Scheube (2) in his work on tropical diseases gives an account of the post-mortem conditions commonly found in uncinariasis. There may or may not be emaciation associated with anemia, the heart is often slightly hypertrophied, the myocardium is soft and fatty. The liver and kidneys but seldom amyloid, are usually fatty; the stomach presents a chronic catarrhal condition at times with considerable dilatation. the mucosa of the ileum and jejunum contains numerous small petechiæ, dark red if recent or slate colored if old. In cases of recent development the mucosa may be covered with fresh blood, but this is uncommon where the disease is of long standing, even in the presence of numerous parasites. Parasites are often found attached at the center of the petechiæ or a break in the mucosa may indicate a point of previous attachment. Hemorrhages of considerable extent may occur into the submucosa, and Bilharz and Grassi are quoted as having found parasites in the submucosa rolled up and surrounded by such collections of blood. Sandwith, however, found parasites upon several occasions with a half of their body buried in the submucosa. From this it is supposed that Bilharz's and Grassi's observations are to be explained by the activity of the worm in penetrating the mucosa rather than as an intracorporeal development of the embryo.

The intestinal mucosa may be thickened and the solitary follicles, Peyer's patches and mesenteric glands enlarged. There is said to be very profound anemia of the brain. Wucherer has reported a case of adhesive peritonitis associated with the presence of uncinaria in the intestine. Marius and Francete state that the bone-marrow is in a condition similar to that seen in pernicious anemia.

Williams (3) observed a perforation high in the small intestine at the site of an old cicatrix and a number of round scars in duodenum and jejunum suggesting ulcerations.

Fearnside (4) in necropsies on 78 cadavers containing uncinaria found that 60 per cent showed in the mucosa areas of congestion several centimeters in diameter and 11 per cent had small erosions and ulcerations 1-2 mm. in diameter.

Strong (5) in a case showing at necropsy a large number of parasites describes in sections from the small intestine an eosinophilic infiltration of the mucosa of the muscularis mucosæ and part of the submucosa. Certain of these eosinophiles are increased in size, and contain large red swollen granules of a vesicular appearance. Breaks in the mucosa extending downward to the submucosa were found. These were surrounded by areas of leucocytic infiltration and hemorrhages and were supposed to be caused by the parasites, though none were found in the section examined.

The changes in the blood and the factors in the causation of these changes are of very great interest and practical value. It has been held that the anemia is due merely to the abstrac-

tion of the blood from the intestine by the parasites. Against this may be urged the fact that the anemia does not always vary directly with the number of *uncinaria* present in the intestine. Cases of profound anemia with a comparatively small number of parasites are on record. Besides this there is evidence that there is an absorption of some toxic substance. The existence of a deposit of blood pigment in the liver is in favor of some hemolytic agent being present, as is the occurrence of necrosis there an indication of an actively toxic agent. Mallory (1) has been able to produce experimentally the form of necrosis present in this case, a necrosis limited to the centre of the lobules, and he thinks this variety rather than the irregularly disseminated foci of smaller size represents the action of a toxine. Rake (6) has demonstrated in five cases of *uncinariasis* that the amount of iron present in the liver post-mortem is less (about $1/7$) than that found in pernicious anemia. However, there is a considerable quantity of blood lost to the body and this taken with the low color index seen in *uncinaria* cases would seem to offer sufficient explanation for such results. Roger (7) points out that this color index is about $\frac{1}{2}$. Ashford's (8) counts made from 19 Porto Rican cases give an average color index of about 6/10. In the most severe types the conditions of a primary anemia are simulated.

Calamida (9) has shown that an extract made from the body of certain tape-worms obtained from dogs is capable of producing death in dogs and guinea-pigs by intoxication with fatty degeneration of the liver when injected into circulation or directly into the liver. This extract (in normal saline solution) has a definite hemolytic action on the red corpuscles in test tubes kept at 37° . Nucleated red corpuscles appear in the peripheral circulation should the animal survive after inoculation with this material, and also a leucocytosis is produced in which the eosinophiles predominate.

The association of an eosinophilia with intestinal parasites in man has been observed for several species by Bücklers (10) (*Uncinaria*, *Anguillula*, *Tinea saginata*, *Tinea solium*, *Ascarides*, *Oxyuris*), but whether there is a characteristic leucocytosis in *uncinariasis* or not is not certain. According to Lutz (11) there is none, but this writer thinks that later in the course of the disease there is a relative increase in the number of the white cells, though actually there is a reduction. Roger (7) gives 1-524 as the ratio of white to red cells. In Ashford's (8) 19 cases a leucocytosis of over 10,000 was present in but two, the number was below 5000 in four, while the average of white to red cells was about 1-290. In the published blood-counts there is no apparent relationship between the anemia and the leucocytosis, and a high leucocyte count is present in perhaps less than one-half the cases.

The causation of the eosinophilia is open to a fairly satisfactory explanation. The presence of intestinal parasites in man (and animals) is frequently accompanied by an increase in the eosinophiles of the blood and this increase is caused by many forms of parasites. It was first observed in individuals harboring *uncinaria* by Müller and Rieder (12) in 1891. Later Zappert (13) observed in association with eosino-

philia, the presence of Charcot-Leyden crystals in the stools of two individuals infected with *uncinaria*.

Bücklers' (10) investigation of the relative frequency of eosinophiles and Charcot-Leyden crystals in the stools of persons suffering from intestinal parasites apparently established a definite relationship of the one to the other, and it was found that after the administration of an anthelmintic the persistence of Charcot-Leyden crystals in the stools indicated that the parasites had been incompletely removed.

Leichtenstern (14) found in a fatal case of *uncinariasis* that in these parts of the intestine where the worms were the most numerous were to be found the largest number of Charcot-Leyden crystals. Bücklers (10) advanced the theory that the crystals were an index of metabolic products of the parasites, perhaps of a toxic nature, which products, upon absorption cause, as suggested by Neusser (15) the blood changes (eosinophilia, hemolysis, etc.). According to Leichtenstern crystals are constantly present in the stools of individuals suffering from *uncinaria* or *anguillula* and are frequently found with other forms of intestinal entozoa. The crystals may be hard to find and may be only discovered after a laxative (preferably calomel), which brings away the intestinal mucus in which they lie.

A slight increase in the number of leucocytes with eosinophilic granulations in the blood is common and a considerable increase not rare. For example, Ashford (8) in his 19 cases found nine showing over 8 per cent of the leucocytes present, the highest being 40 per cent, the lowest was 2 per cent. It appears to be established that an increased number of eosinophiles is a common phenomenon with a variety of intestinal parasites. According to Ehrlich and Lazarus (16), if other conditions with an associated eosinophilia are investigated but one explanation applicable to all can be found, namely, that the increase in the number of these cells is the result of chemotaxis. For example, in asthma, as pointed out by Gollasch, there is an eosinophilia together with the appearance of eosinophilic cells and Charcot-Leyden crystals in the sputum, and Van Noorden finds that the number of eosinophile depends directly upon the frequency and recent occurrence of the attacks, not on some lasting constitutional peculiarity, but upon the local action of an inflammatory irritant, since in other individuals having eosinophilia there are no eosinophiles in their sputum.

In a pemphigus case, Neusser showed that the bullæ contained cells which were nearly all eosinophilic, but on producing artificially by a vesicant another vesicle on the same individual, the cells were entirely neutrophilic. In Dühring's disease (*Dermatitis herpetiformis*), Leredde and Perrin demonstrated that at first when the vesicles are clear they contain principally eosinophiles, whereas later, after auto-infection, postules develop and the cells are neutrophilic.

Calamida's (9) work, already referred to, shows in a striking manner the chemotactic influence upon the eosinophilic cells of products obtained from an animal parasite. Capillary tubes containing a sterile normal saline solution of an extract made from the bodies of tape-worms were inserted beneath

the skin of a dog; after a short time they became filled with cells, the majority of which were eosinophiles.

There are two possible sources for a substance positively chemotactic for eosinophiles: (a) it may be a product of the parasite; (b) it may be produced within the body by metamorphosis or degeneration of tissues.

Ehrlich and Lazarus (16) observed that the changes in epithelial and other cells seem to have some relationship to such a positive chemotaxis. In certain skin affections: with atrophic conditions of the gastric, intestinal and bronchial mucosa; with some carcinomata; in lupus foci after tuberculin injection, etc., collections of eosinophilic cells occur about areas of tissue degeneration.

The facts already cited indicate, however, that the accumulation of eosinophiles with uncinaria is the result of a specific chemotactic action of parasites attracting them to the intestinal wall and causing an increase of their number in the blood and in the spleen. That the toxic substance causing the hemolysis in uncinariasis is not identical with that producing the eosinophilia is probable, since the anemia and eosinophilia bear no constant relationship to one another. In the case here reported the toxic substance which caused the central necrosis in the liver was not positively chemotactic for eosinophiles which were scant in number in the necrotic areas, though polynuclear leucocytes were present.

The inverse ratio that exists between eosinophiles and neutrophils in clinical observation has led to the belief that substances positively chemotactic for the one may be negatively chemotactic for the other.

Leichtenstern had a case of severe uncinariasis with an eosinophilia of 72 per cent. Croupous pneumonia supervened and this percentage dropped to 7 per cent, rising to 54 per cent after recovery from the pneumonia and falling to 11 per cent after anthelmintic treatment; a year later it was 8 per cent with a few worms still present. (In a case of trichiniasis occurring in Dr. Osler's service (T. B., Gen. Med. No. 11,387) with an eosinophilia of 37 to 44 per cent and 54 to 48 per cent polymorphoneutrophils, showed after onset of an acute lobar pneumonia, eosinophiles 24 per cent and neutrophils 67.4 per cent. The eosinophilia had disappeared a month later (4.5 per cent).

Of the origin of the eosinophilic cells themselves there are but three possibilities. That they spring from similar or heterogeneous cells of the blood, or from the fixed tissue cells elsewhere and are transported by the blood, or locally at the site of the eosinophilic infiltration.

If they were the products of the proliferation of blood-cells, one would expect to find in the eosinophilic cells in the peripheral circulation signs of (1) cell division and (2) transitional forms between other cells and those with the eosinophilic granulation. No positive evidence of cell division in the peripheral circulation has been offered. Transitional cells, too, are not seen, though in leukemia cells do occur which have polychromic granulations.

Ehrlich states that in the bone-marrow all stages of transition are to be seen from specific mononuclear cells with

granules to the polymorphonuclear varieties, with either neutrophilic or eosinophilic granulations, as the case may be. During this transition there is a change in the character of the granules also, the younger cells have basophilic granulations in excess which diminish proportionately to the advance of the "ripening" of the cell. Only the mature or ripe cells appear in the circulating blood. The maturing or ripening of both the cells and granules is normally equally advanced. Under abnormal conditions, as in leukemia, the cells ripen faster than the granules and thus ripe cells with unripe granules may get into the circulation. These unripe granules take a blackish stain with eosin-aurantia-negrosin, or bluish-red or blue with eosin-methylene blue. Such cells with unripe granules are in no way transitional but are *immature forms*, and it is easily possible that an abnormally rapid formation of eosinophiles by the bone-marrow would permit of the entrance of these atypical elements into the circulation.

The evidence that eosinophiles are formed in organs other than the bone-marrow is not conclusive. Mononuclear granular cells are not found in lymphatic tissue, and in the spleen, as in the blood, evidence of cell proliferation and transitional forms is not found. The removal of the spleen far from causing any decrease in the proportion of eosinophilic cells, causes a distinct increase.

There is even less evidence that eosinophiles are formed locally within the foci where they are found accumulated. Mastzellen, as Ehrlich and Bäumer (16) have shown, may be formed locally, but there is no proof that eosinophiles can, *i. e.*, the existence of cell proliferation or of transitional forms.

Brown (17) from his observation on cases of trichiniasis came to the conclusion that the eosinophiles might be formed locally from the neutrophils. He observed forms typical of neither and thought to be transitional, and concluded that the change possibly took place in the muscles (locally) as the proportion of eosinophiles was there greater than in the circulating blood. He also thought that the change did not take place in the circulating blood.

It is easily understood, accepting Ehrlich's theory of ripe cells with unripe granules, that it would not be difficult to mistake a cell with unripe granules for a transitional form. Moreover, in the trichiniasis case reported above from the Johns Hopkins Hospital, the cells in the blood were not at first characteristic of typical eosinophiles, and the same question arose as to the possibility of their being transitional forms. Later, before the eosinophilia subsided, they became perfectly typical. A plausible explanation seems to be that these cells were of the nature Ehrlich described. Brown's finding of an increased number of eosinophiles near the parasites in the muscles could be as well, and perhaps better, explained on the theory of chemotaxis.

It seems reasonable to suppose that in cases of infection with *Uncinaria duodenalis* the parasite produces in the intestinal canal a substance which is positively chemotactic for eosinophilic leucocytes, thus causing a local infiltration of the intestinal structures with eosinophiles and at times an accu-

mulation of eosinophiles in the blood. It is probable that there is formed another toxic substance which causes hemolysis and tissue degeneration.

Blanchard (18) refers to reports upon *Uncinaria duodenalis* in the United States as early as 1830 by Chabert, and in 1845 by Duncan, describing an anemia among the negroes in Louisiana; Lyell in Alabama, Heusinger and Giddings in South Carolina were also mentioned. Little and Leatherman made some doubtful reports of the existence of *uncinaria* in Florida.

The following definite cases are on record:

CASE 1.—Blickhahn (19) reported from Missouri in 1893.

The disease was contracted in Germany, the patient recovered. The red blood-corpuscles were only 800,000 to the mm., a marked leucocytosis was present and the hemoglobin was low. The presence of alpha and gamma granulations in considerable numbers awakened a suspicion of myelogenous leukemia.

CASE 2.—Herff (20) reported from Texas in 1894.

The disease probably was contracted in Mexico. The diagnosis was made post-mortem. No blood count was given. Also several indefinite cases among Italians, which were only diagnosticated symptomatically.

CASE 3.—Möhlau (21) reported from Buffalo, New York, in 1896.

The source of disease was not stated. Recovery occurred. The red blood-corpuscles were 4,500,000 to mm. No other blood estimations were given.

CASE 4.—Same.

The disease was contracted in New York and traced to foreign laborers. Recovery followed. No blood counts were given.

CASE 5.—Same.

The source of disease was not stated. Recovery took place. No blood counts were given.

CASE 6.—Same.

The disease was contracted in New York and traced to foreigners. Recovery took place. No blood counts were given.

CASE 7.—Same.

Disease contracted at St. Gotthard. Unimproved. No blood counts were given.

CASE 8.—Tebault (22) reported from Louisiana in 1899.

The disease was contracted in New Orleans. Recovery took place. The red blood-corpuscles were 2,500,000 to mm., the white cells were 30,000. The patient also had malaria.

CASE 9.—Dyer (23) reported from Missouri in 1901.

Source of disease was not stated. Recovery took place. No detailed blood count was given.

CASE 10.—Claytor (24) reported from the District of Columbia in 1901.

The disease developed in Virginia. Recovery took place. The red blood cells were 1,577,000 and white cells 4400 to mm. The hemoglobin was 30 per cent, the eosinophiles were 5 per cent of the leucocytes present. No nucleated red

cells were seen. (Patient has since died from cerebral hemorrhage.)

CASE 11.—Allyn and Behrend (25) reported from Pennsylvania in 1901.

The individual contracted the disease in Italy. Recovery took place. Red blood cells were 1,220,000 and the white cells 8650 to mm.; hemoglobin was 15 per cent.

CASE 12.—Gray (26) reported from Virginia in 1901.

The disease was contracted in Virginia. Recovery took place. No blood count was given. A sister of this patient was suspected of having the disease; diagnosis was based purely on symptoms, neither ova nor parasites were observed.

CASE 13.—Schaeffer (27) reported from Texas in 1901.

The disease was contracted in southern Mexico. Recovery took place. The red blood cells were 2,970,000 and the white cells were 14,300 to the mm. Hemoglobin was 57 per cent and the eosinophiles 6 per cent of the leucocytes present. There were also *amœbæ coli* and ova of *trichocephalus dispar* in the stools.

CASES 14 AND 15.—Same.

Two students; both probably recovered; both had eosinophilia; one had malaria. No other notes were given.

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- (25) Allyn & Behrend: American Medicine, June 13, 1901, p. 63.
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DISCUSSION.

DR. TRAYER.—This is, so far as I know, the first case of this disease which has been recognized in Baltimore, despite the fact that for several years we have had our eyes well opened to the probability of its occurrence in these regions. The fact that in the past four years we have observed in this hospital three cases of diarrhea associated with *Strongyloides intestinalis*, a parasite which is found under very much the same conditions and often in association with *Uncinaria*, has led us to expect that we should soon discover cases of this nature. This parasite was first observed by Dubini in 1838 in the intestinal tract of a young woman dying in a hospital at Milan. The recognition of its pathological importance dates from Griesinger's discovery in 1851, that it was the cause of the so-called Egyptian chlorosis, a very grave and often fatal form of anæmia prevalent in Egypt. The worm became an object of yet greater interest to the medical world in 1880, at the time of the excavation of the St. Gothard tunnel. Among the tunnel-workers there developed an anæmia associated often with diarrhea and occasionally with bloody stools, which presented many of the features of progressive pernicious anæmia. The dejecta of these patients were found to contain numerous eggs of *Uncinaria*, together often, with embryos of the allied *Strongyloides intestinalis*. The disease was studied by Perroncito, Sahli, Bozzolo and Pagliani, Grassi and others. While the eggs of *Uncinaria* and those of *Strongyloides intestinalis* are extremely similar, indeed, scarcely to be distinguished, those of the former alone appear in the stools; the eggs of the *Strongyloides* hatch within the intestinal tract excepting in very rare instances. In several cases of infection with *Strongyloides intestinalis* studied carefully for months, we found myriads of larvæ, but only two eggs. The larvæ of *Strongyloides intestinalis* when first passed are from 200-400 μ in length and extremely active. They are in many ways similar to those of *Uncinaria*, which, however, are never found in the fresh stools. The eggs of *Uncinaria duodenalis* are elliptical structures from 55-60 μ in length by 30 μ in breadth, and when passed are in the stage of segmentation. From twelve hours to two or three days after passage, if kept at about 25° C., the larvæ begin to escape, and after four to eight days reach the limit of development of which they are capable outside of the human body. It is probable that in most instances they are introduced into the organism through water, uncooked vegetables, or by the hands themselves. While the disease is widely spread in Europe, Asia, Africa, South America and in the Antilles, but few cases have been reported in this country. The disease is especially common among miners, brick-workers and tunnel-workers. While infection with *Uncinaria duo-*

denalis results in grave and often fatal symptoms, *Strongyloides intestinalis* is a much less malignant parasite, being associated, in the majority of instances, with chronic diarrheas, which, when properly treated, are rarely fatal; often, indeed, the parasite may be present for long periods of time without producing any symptoms.

The importance of recognizing the eggs of *Uncinaria duodenalis* in the stools is great, in view of the fact that the worms may be easily expelled. Treatment with large doses of male fern or thymol causes the entire disappearance of the parasites with recovery. It is an interesting fact that while the symptoms associated with the presence of *Strongyloides intestinalis* are much milder, and amenable often, to treatment by general measures such as are adopted in any case of chronic diarrhea, yet it is often extremely difficult to rid the patient of the worms; the treatment which is so efficacious in the case of *Uncinaria* is often almost wholly ineffectual in the case of *Strongyloides*.

The occurrence of this case should emphasize the great importance of systematic examinations of the stools, particularly in cases of grave anæmia.

NOTES ON NEW BOOKS.

The Principles and Practice of Medicine, designed for the use of practitioners and students of medicine. By WILLIAM OSLER, M. D., F. R. S., F. R. C. P. (Lond.), Professor of Medicine in the Johns Hopkins University, etc. Fourth Edition, pp. 1-1182. (New York: D. Appleton & Co., 1901.)

In his preface to the fourth edition of his text-book the author says: "Dysentery, yellow fever and the plague have attracted the attention of so many workers that it is difficult to keep pace with the rapid progress of our knowledge." But that he believes that this statement, to a large extent, holds true for many other diseases, is shown by the long list of articles, given a little later, which are wholly or partially new. In fact it may be said that any one who is seeking for a striking concrete example of the advances that are being made in medicine every year, as the result of combined clinical and experimental studies, could hardly do better than note carefully the numerous additions and changes which have been found necessary in order to bring up to date a work, the last edition of which appeared barely three years ago. But in order that a book shall serve as an every-day text-book and not be in the main a work of reference, the author is ever hampered by the fact that while nothing of real importance must be omitted and while the various subjects must always be treated of in a readable form but at the same time comprehensively, any undue expansion in the eyes of the student, as well as of the publisher, will inevitably be looked upon as the unpardonable sin. An intuition, inborn to a certain extent perhaps, but mainly the outgrowth of years of clinical and pathological experience, has enabled Dr. Osler to meet these difficulties successfully, and thanks to his broad grasp of the various fields included in his subject he has pruned judiciously, sifted the essentials from the non-essentials and utilized to their full extent the rich but often cumbersome and confused masses of material with which he has had to deal. As a result we have the same compact volume as before, but containing within its covers an added wealth of reliable data.

Of the general characteristics of the work, sufficient has

been said as long ago as 1892, in the brief review which appeared in these pages at that time. In the present edition, the dearly bought knowledge of various diseases (typhoid, malaria, dysentery, etc.) which has accrued from the Spanish-American, South African and Philippine campaigns, as well as from some of our home epidemics (notably that of typhoid fever in Philadelphia), has been summarized and the lessons to be learned therefrom clearly and succinctly stated. Pneumonia, small-pox and cerebro-spinal fever have not been neglected, and new points in treatment and diagnosis have been added.

The anemias have been worked over again, and in the brief but clear description of splenomegaly, some of the author's recent clinical experience has been introduced. Herpes zoster has been definitely classed with the acute infections processes. The subject of arsenical poisoning has been enriched by the results of studies aroused by the Manchester epidemic. The article on aphasia has been rewritten and appears in a much improved form. In short, the fourth edition shows everywhere the unmistakable signs of a careful revising hand, and if Dr. Osler has not accomplished the impossible, at any rate he has come within a reasonable distance of so doing. The publishers have done their work well and may be congratulated on the general appearance of the volume.

The History of Medicine in the United States. A Collection of Facts and Documents relating to the History of Medical Science in this Country, from the earliest English Colonization to the year 1800, with a Supplemental Chapter on the Discovery of Anæsthesia. By FRANCIS RANDOLPH PACKARD, M. D. Illustrated. Octavo, 542 pages. (Philadelphia and London: J. B. Lippincott Co., 1901.)

This most interesting work, which has occupied the author for many years, is, as he says, the first attempt at a general history of medicine in this country. He is very modest in his claims for it, saying in his preface that "it should be regarded rather as a series of essays and compilations, than in the light of a continuous historical work." It could not be supposed that an attempt to cover so large a field, when the sources of information are limited, scattered, and in many cases almost inaccessible, should succeed at once. It will require much time and effort to realize one's ideal of such a work. Nevertheless here is a good beginning of the difficult task and we cannot be too grateful to Dr. Packard for all his labor (doubtless to be but poorly requited, as all such labor is), in bringing together and rendering available so much of the early medical history of our country.

The typographical execution of the work is all that could be asked. The illustrations number 25, the frontispiece being a cut of the Pennsylvania Hospital, opened on the 6th of February, 1752. The other illustrations are mostly portraits of eminent physicians, 12 of whom are Philadelphians, 4 from Massachusetts, 1 each from New York, Connecticut, New Jersey, Maryland and Georgia. The two last States are represented by Charles Frederick Wiesenthal (reproduced from this BULLETIN for July-August, 1900) and Crawford W. Long. The remaining illustrations are: Edinburgh Certificate of Dr. Asheton of Philadelphia, Surgeon's Hall, Philadelphia, Fac-Simile of the contract between the Pennsylvania Hospital and the Continental Army Surgeons for the use of the "Elaboratory" of the Hospital by the latter, students' Certificate conferring the right to attend the Practice of the Pennsylvania Hospital, seal and corner-stone of the Pennsylvania Hospital, Fac-Simile of the First Medical Publication in the colonies of North America, and the First Public Demonstration of Ether Anæsthetization by Dr. W. T. G. Morton at the Massachusetts General Hospital on

October 16, 1846. We would suggest to the author to add to these in any future edition, which is certain to be called for, portraits of the great New England surgeon, Nathan Smith, of the patriots Joseph Warren, of Massachusetts, James McHenry, of Maryland, Hugh Mercer, of Virginia, and John Moultrie, of South Carolina. David Ramsay, the historian, of Charleston, ought also to be included, and there are several from Maryland besides McHenry who would honor the book, as John Archer, of "Medical Hall," Harford Co., the 1st graduate, a distinguished medical teacher and a statesman of note, Upton Scott, of Annapolis, first President of the Medical and Chirurgical Faculty of Maryland, Ennalls Martin, "the Abernethy" of Talbot Co., surgeon in the Revolution, Henry Stevenson, of Baltimore, the great inoculator, Charles Alexander Warfield, the first to propose a separation from the mother country and leader of the Peggy Stewart burning at Annapolis, and John Crawford, unquestionably the ablest physician of his day, the introducer of vaccination into Maryland, a founder of the Society for Useful Knowledge, 1798, and of the Baltimore General Dispensary 1807, Grand Master of Masons, 1801-13, who earnestly advocated the germ theory and practiced antiseptically over 100 years ago. There should also be illustrations of the earliest medical schools.

The headings of subjects are comprehensive, embracing, besides medical events in general, medical education, epidemics, medical schools, hospitals, societies, the Revolutionary War, bibliography, legislation and the discovery of Anæsthesia. An appendix contains: The Examination of Dr. Church, Dr. John Morgan's Memorial, the Pennsylvania Hospital and Reminiscences of the Physicians and Surgeons who have served it, by Dr. Charles D. Meigs, List of Authorities, and Medical Societies founded in the United States, before the year 1825.

In connection with the above, we would call the author's attention to some Maryland events which might have been included. Dr. Thos. Gerard, of St. Clement's Manor, arrived in Maryland in 1638 and took a prominent part in the events of his day; see Thomas' recent history. Dr. Luke Barber somewhat later was equally prominent and was mediator in the battle between the Puritans and Royalists at Providence (Annapolis), March 26, 1655. The Drs. Gustavus Brown through three generations (1708-1804) held a distinguished place in Maryland, all being Edinburgh scholars and two of the three being summoned to Washington in his last illness. The medical school projected in Baltimore in 1789, while it failed, deserves some mention, resulting in courses on obstetrics and anatomy, by Drs. George Buchanan and the younger Wiesenthal. There were many Maryland physicians eminent in the Continental Army, and if the surgeons of Connecticut or the other colonies are mentioned, we see no reason why the Marylanders should not be included also. Of medical societies some mention should be made of the Baltimore Society of 1788-'90, of the Harford Medical Society, founded by John Archer and his pupils at "Medical Hall," April 1st, 1797, and of the Maryland Society for Useful Knowledge, founded December 13, 1798, by Jos. Priestley, John Crawford and others, before which a large number of medical papers were read between 1798 and 1806. The Maryland Hospital was founded at Baltimore, February 20, 1798, as a general hospital, including the insane, and fulfilled here the same rôle as the Pennsylvania Hospital until 1828, when it became the Maryland Hospital for Insane, under which title it still exists.

In connection with the founding of the Medical and Chirurgical Faculty of Maryland, it was hardly fair to give it just *five* lines in a section embracing 55 pages. And, in connection with the subject of vaccination, we cannot see how Dr. James Smith, of Baltimore, can be omitted, who, while not actually the first to practice it (he first used it at the almshouse, May 1, 1801), probably did more than any one to spread

it over the country and make it known to the profession and people, establishing as early as March 25, 1802, a vaccine institute, which later became a State and then a national institute. One of the objects of this institute was to provide vaccine virus gratuitously for the poor. "The services of this physician in promoting the introduction and spread of this great boon and in arresting repeatedly epidemics of small-pox, entitle him to the eternal gratitude of this community." Nor is Dr. Smith alone to be mentioned; the profession throughout the State was full of zeal in behalf of the great discovery, in their eagerness to secure its adoption offering pecuniary rewards to those who would submit to its performance. It may also be mentioned that the Medical and Chirurgical Faculty early gave the new discovery its formal approval and was perhaps the first medical organization in the country to do so.

As we have already indicated, the work is rather open to criticism on the ground of omission than of commission. To the writer, the thrilling accounts of the several epidemics of yellow fever in Philadelphia, and the sketch of the medical department of the Continental Army were the most interesting parts of the book. The latter especially threw a new light upon our Revolutionary struggle and made clearer the difficulties under which our forefathers labored and their merits in persevering through the long and terrible sufferings which they endured. "Just think of Dr. Morgan's being unable to dole out more than two scalpels to the surgeon who was to have charge of the wounded in what it was anticipated would be a bloody battle, and of the suggestion that a razor should be used instead of a scalpel."

At page 62, under the heading, "The Earliest Recorded Autopsies in America," it is said that the earliest mention of an autopsy here is to be found in "An Account of Two Voyages to New England," published at London, in 1674, by John Josselyn, an Englishman, who had spent some time in New England. It was that of "a young maid who was troubled with a sore pricking at the heart, still as she leaned her body or stept down with her foot to the one side or the other." She died, and her friends, desirous of discovering the cause of the trouble, had the body opened, whereupon "they found two crooked bones growing upon the top of the heart which, as she bowed her body to the right or the left side, would jab their points into one and the same place, till they had worn a hole quite through." Doubtless there were many cases in the older colonies before this, which a search of the records might reveal. The late Dr. John R. Quinan, who was the most indefatigable antiquarian we have ever had in these parts, unearthed several from the Maryland records. In 1642 he found a report of an "Enquest taken at St. Maries upon the view of the body of Ann Thompson." In 1643, he found an "Enquest on an Indian ladd killed by John Dandy," the report being signed by "George Binx, Foreman," who elsewhere is styled "Licentiate in Physicke." On September 24, 1657, an inquest was held on Henry Gouge, at Patuxent, "by Rd. Madocks and Emperor Smith, Chirurgeons, by order of the Councel," the chirurgeons being allowed one hogshead of tobacco each as fee. On August 8, 1670, an autopsy was done "by John Stanley and John Peirce, Chirurgeons," on the head of Benjamin Price, who had been killed by Indians. (M. S. Council Book.) In 1671 an act was passed allowing 250 pounds of tobacco to the coroner for an inquest. An examination of the records at the Historieal Society might multiply these instances.

Of "Juries of Women" (p. 59, not given in the index), there are several recorded in Maryland earlier than those given by the author. In 1652, a jury of matrons decided as to the alleged pregnancy of a murderess. In 1656, a similar jury

decided as to a case of supposed pregnancy, and another as to an alleged infanticide. In 1658, a jury of women was ordered by the Court of Kent County to report upon a case of alleged infanticide, and rendered through their forewoman, Mary Vickers, a verdict "that the accused, Hannah Jackson, is clear from the bearing and never had a child." In 1659, a similar jury decided as to the pregnancy of a woman convicted of felony, etc., etc.

The brief allusion to the two voyages of Capt. John Smith from Jamestown, in 1608, recalls the interesting descriptions written of them by the physicians accompanying—"Walter Russell, Gentleman, doctor of physicke," and "Anthony Bagnell, Chirurgeon." Smith on these occasions thoroughly explored the Chesapeake Bay, and even entered the Patapsco River, probably beholding the site of the City of Baltimore. From the resemblance of the clay on the river banks to "bole armoniack (terra sigillata)," they called it the "Bolos." By the way, this article is mentioned at p. 20 of Packard's book in "Receipts to Cure Various Disorders," 1643. Smith was in search of a northwest passage, and the physicians, being the educated men of the parties, were appointed to draw up the accounts of the expedition, which they signed with their names, as may be seen in Smith's General History, Chap. V.

At p. 160, it is stated that the first to receive a medical diploma in North America was Daniel Turner, who was thus honored by Yale College in 1720, on account of his benefactions to the college. As the medical department of Yale was not founded until 1813, it would be interesting to know whether it possessed the *legal* right at this time to confer such a degree. Of course, if it had not, such action was invalid. We do not know of another such case. Would Princeton, Washington and Lee, Haverford, etc., be able to confer a medical degree now?

At p. 161, Dr. John Archer's diploma is reproduced, "probably the first medical diploma awarded after a course of study in America." It was issued in 1768 by the "Collegium et Academia Philadelphiensis," and, as is well known, forms one of the treasures of the Medical and Chirurgical Faculty of Maryland. It is unfortunate that more care was not taken in reproducing this important document, which ought to have been given in *fac-simile*. A *fac-simile* of it was readily available in the Centennial number of the Maryland Medical Journal, April 29, 1899. Numerous mistakes occur in the author's copy, some of which are "pervenorint," "ingenum," omission of the words after "Archer"—"apud nos Praelectionibus in medicina omnium Professorum"—"Vigillissimo," "Liberis," "majori," "Johannem," "Acadae," "Angi," "clinicus," "Praxeos," "in" omitted before "nosocomio," etc. These errors are easily seen by referring to the *fac-simile*.

At p. 36, it is said that Dr. John Glover, of Massachusetts, received the degree of M. D. at the University of Aberdeen about 1650. We doubt very much if that degree was given at Aberdeen until long after that date. The medical school was not established until about the middle of the 18th century, and we have before us the diploma of Dr. James Walker, of Maryland, dated at Aberdeen, December 31, 1724, and signed by Drs. Gregory, Donaldson, Skeene and Burnett, but not conferring any degree.

The following "first" things will probably be of interest to the reader: 1st medical society founded in Boston in 1735, lasted six years; 1st State Society founded in New Jersey in 1766, and still in existence, although with a break from 1795 to 1807—six State societies were founded before 1800; 1st dispensary founded in Philadelphia in 1786; inoculation for small-pox introduced into England by Lady Mary Wortley Montague, April, 1721, and on June 27, 1721, Dr. Zabdiel Boylston inoculated successfully his only son and two negro servants; vac-

ination was introduced into America in the summer of 1800 simultaneously by Dr. Benjamin Waterhouse, of Boston, and Dr. John Crawford, of Baltimore; the 1st vaccine institution—"Institution for the inoculation of the Kine Pock"—was organized in New York City on January 11, 1802 [Dr. James Smith's coming two months later]; 1st feetable that of the New Jersey Society, 1766; 1st medical college instituted in Philadelphia in 1765; 1st course of lectures on the practice of medicine, delivered by Dr. John Morgan, 1766; 1st medical publication—Thacher's "Brief Rule on Small Pocks"—1677; 1st official pharmacopœia issued under the auspices of the Massachusetts Medical Society, 1808 (a private pharmacopœia had been published at Lititz, Pa., by Dr. William Brown, of Charles Co., Md., in 1778); 1st course of clinical lectures, delivered by Dr. Bond (a Marylander), at the Penna. Hospital, 1766; 1st use of anæsthetics in surgical operations by Dr. Crawford W. Long, of Georgia, March 30, 1842.

At p. 11 it is said Mr. Pratt was appointed surgeon to the plantation (Mass.), March 5, 1682, and on p. 12 we are told that the same gentleman was shipwrecked and drowned in 1645! At p. 90 it is said vaccination was announced by Jenner in 1779! "Occasional" is used for "occasion" at p. 194. We feel sure that the critical Dr. Holmes never penned "Albinus" and "Gaubrus," p. 231. Inoculation was *not* introduced in 1712, p. 432. As we have already intimated, some additions will have to be made to the seventeen medical societies founded before 1800, p. 525. In the list of authorities "chiefly consulted," p. 521-5, we note but one from Maryland—McSherry's History of Maryland; and in the entire index of sixteen pages there are but thirteen allusions to Maryland doctors!

A "medical history of the United States" cannot be limited to a few centres, however important the part they have taken in medical progress may appear. The historian must write for all and without bias. One circumstance alone, that among the names of sixty-three Americans in the list of graduates in medicine in the University of Edinburgh between 1758 and 1788, Stillé found "that but one of these students came from the New England Colonies" (p. 156), indicates that there must have been many eminent men in the Middle and Southern Colonies who left their impress upon their age, by reason of the standing and acquirements which such a training secures. That Maryland has deserved more attention than the author has given it we have furnished good evidence, and we feel sure he will be richly rewarded for his trouble if he will consult the historical records of this State, and especially Quinan's Annals of Baltimore, the Maryland Medical Journal, THE JOHNS HOPKINS BULLETIN, and the forthcoming "Medical Annals of Maryland"—the Centennial Memorial of the Medical and Chirurgical Faculty of Maryland. E. F. C.

A Text-Book of the Practice of Medicine by DR. HERMAN EICHHORST, Professor of Special Pathology etc., Zurich. Authorized translation from the German. Edited by AUGUSTUS A. ESHNER M. D., Professor of Clinical Medicine, Philadelphia Polyclinic. With 84 illustrations; 2 volumes. (Philadelphia: W. B. Saunders & Co., 1901.)

The above translation as appears from the advertisement is a condensed edition of the author's larger work on Special Pathology and Therapeutics. The book presents in general the usual characters of a text-book on the Practice of Medicine, but the author has added chapters on diseases of the bladder, the male sexual organs and skin diseases. Reference is much facilitated by the employment of five different types. Although the book contains about twelve hundred pages the individual chapters are brief. The diseases accompanied by an elevation of temperature are illustrated by fever charts

which are written sometimes in centigrade scale, sometimes in Fahrenheit. When temperatures are mentioned in the text they give the usual American scale of Fahrenheit as well as the German scale of centigrade.

An especially valuable feature of the book is that it gives the methods of making clinical and microscopic tests, in their appropriate places, such as the method of staining for the gonococcus, chemical examination of the stomach contents, the tests for sugar in the urine, etc.

Special attention is given to treatment. Medicinal treatment is written in English in the form of prescriptions, and the doses of drugs employed are given, both in the metric and apothecary systems.

The paragraphs on the European watering places and baths will be of especial interest and value to Americans.

In a few places the statements will be found rather unclear. For example (vol. i, p. 207). "The gastric contents are obtained by expression with the aid of a soft stomach-tube four hours after, and a test meal one hour after, a test breakfast."

And (vol. ii, p. 36). "The internal capsule is the white medullary mass lying to the median aspect of the optic thalamus and the caudate nucleus, and to the lateral aspect of the lenticular nucleus," which must have been reversed in transcription.

Altogether the book is an excellent one of its kind. Its completeness, yet brevity, the clinical methods, the excellent paragraphs on treatment and watering places, will make it very desirable for students, and for practitioners, who have little time to read. E. B. B.

The Treatment of Fractures. By CHAS. L. SCUDDER, M. D., Assistant in Clinical and Operative Surgery, Harvard Medical School. Second edition, revised and enlarged. Octavo, 433 pages, with nearly 600 original illustrations. (Philadelphia and London: W. B. Saunders & Co., 1901.) Polished buckram, \$4.50 net.

A review of the first edition of this excellent work was published in the January BULLETIN. There is little to be added in reference to the present edition except to say that the book has been thoroughly revised. Many X-ray plates have been reproduced to assist in familiarizing the reader with the study of such plates. Numerous other new illustrations have been added, and the book has been considerably enlarged.

Libertinism and Marriage. By DR. LOUIS JULLIEN (Paris). Surgeon of Saint-Lazare Prison; Laureate of the Institute, of the Academy of Medicine, and of the Faculty of Medicine of Paris. Translated by R. B. DOUGLAS. Pages v-169. (Philadelphia: F. A. Davis Company, Publishers, 1914-16 Cherry Street.)

The object of this little book is good; its subject-matter is of vital importance to the health of women, especially married women and mothers; its author has had exceptional opportunities for the observation and study of the effects of venereal disease and the words of warning which he utters against the evils of uncured venereal disease are forcible and earnest. The style of the book, however, is not in keeping with the gravity of the purpose of the writer, and the treatment of the subject is popular rather than scientific. It would have been productive of greater good in America if the topics had been discussed in a higher tone. The translation is not always happy. The book is well printed and attractively bound.

The Proceedings of the New York Pathological Society for the years 1899 and 1900.

Beside the mass of short reports of cases and abstracts of pathological investigations, the volume contains the Middleton-

Goldsmith Lecture by Dr. Flexner on the Etiology of Tropical Dysentery. In this lecture he arrives at the conclusion that the bacillus of Shiga (with which the organism isolated by himself is identical) is of paramount etiological importance, at least, in a great group of cases. Among the various reports, those of Lartigan on Typhoid Uterine Infection, in which he reviews the literature, and on hyperplastic intestinal tuberculosis, are of especial interest. Very ingenious, too, is Hodenpyl's investigation of pneumoconiosis from the chemical standpoint. While the reports are very brief, there is a great deal of instructive and suggestive material contained in the book.

Infant-Feeding in its Relation to Health and Disease. By LOUIS FISCHER, M. D. Containing 52 illustrations, with 23 charts and tables, mostly original. (*Philadelphia, Chicago: F. A. Davis Company, Publishers, 1901.*)

There are many points of interest in this little volume, although the book is so poorly arranged that it is somewhat confusing. It is divided into two parts. The first considers the anatomy and physiology of the infantile digestive tracts, the section on digestive ferments being especially thorough for a text-book of this size. Then follows the chemistry of milk, breast-feeding and kindred subjects, and the modification of cow's milk.

We note with pleasure a number of tests for the adulteration of milk. There are also some very good diets for the nursing mother, although we are somewhat at a loss to understand why zwieback is mentioned in a book apparently intended for American practitioners.

The second part of the work treats largely of feeding by infant foods, and of the diseases arising from deficient nutrition. The chapter on infant-stools is especially to be commended. It is to be regretted that the subject of summer diarrhœas is not considered, and that so little space is allotted to the subject of premature infants and incubation. Few subjects are of more interest.

The author appears very enthusiastic over the Gaertner milk, and strongly condemns the use of laboratory milk. In its place, for cases demanding artificial feeding, he would substitute raw cow's milk, diluted as occasion requires. He states that if pure cow's milk can be obtained, pasteurization and sterilization are more harmful than otherwise. While this is doubtless true, yet, bearing in mind the uncertainty of obtaining pure milk except at the "laboratories," and the hosts of infants affected with summer diarrhœas, it is our opinion that there are few truer friends to the infant than the methods of pasteurization and sterilization now in vogue.

The volume contains many references, mostly to European sources, yet it appears to us somewhat incomplete. We believe that reference to men who feed undiluted cow's milk to children at birth, and to sick infants in the early months of life, had better be omitted (see page 101), and in its stead would substitute mention of those who, like Rotch, Wescott and others, by their careful and painstaking work, have done much to put the study of infant feeding upon scientific lines.

The author has undoubtedly had a wide experience, and we hope to see a second edition of his work, better arranged and free from the errors in proofreading that mar the text.

F. W. L.

A Text-Book on Practical Obstetrics. By EGBERT H. GRANDIN, M. D., with the collaboration of GEORGE W. JARMAN, M. D. Third Edition, Revised and Enlarged. Illustrated with 52 full-page photographic plates and 105 illustrations in the text. Pages xiv-511. (*Philadelphia: F. A. Davis Company, Publishers, 1914-16 Cherry Street.*)

New text-books on obstetrics should present unusually

strong reasons for crowding a field already well filled. The present edition of Drs. Grandin and Jarman's work, although somewhat enlarged and considerably improved, contains nothing which is not found in many other works of similar size, and offers an unusually large number of points for criticism.

A chapter dealing with anatomy and embryology has been added to the volume, but the authors have not taken advantage of recent embryological investigation, and have presented the views of former years, derived from the study of the lower mammals, and disproven in large part by the work of Peters, Spec, Selenka and others.

The recommendation of manœuvres that require a finger in the rectum for delivery in a normal case, is so contrary to all modern ideas of proper technique, that mere mention of it should be sufficient to condemn it. It is also rather remarkable that no mention is made of deciduoma malignum. Lack of space prevents the mention of other omissions.

The illustrations are but fair. They are mostly photographic reproductions, and although well done in some instances, they are badly chosen and do but little to properly illustrate the text.

The volume must necessarily suffer unfavorable comparison with other obstetrical text-books of similar size and cost.

F. W. L.

Obstetric and Gynecologic Nursing. By E. P. DAVIS, A. M., M. D., Professor of Obstetrics in Jefferson Medical College and Philadelphia Polyclinic. 12mo, volume of 402 pages, fully illustrated. (*Philadelphia and London: W. B. Saunders & Co., 1901.*)

This is an exceedingly attractive little volume. Dr. Davis has presented the subject in a very pleasant manner, and without going into details as to the mechanism of labor, or the mechanical steps of surgical procedures, he has embodied the objective points in an instructive way. The observance of aseptic technique is everywhere emphasized, and the duties of the nurse in various emergencies are presented in careful detail. The appendix contains a short dietary, and methods for the preparation of surgical supplies.

The book should be of value not only to the nurse but to the physician.

F. W. L.

The Acute Infectious Diseases of Childhood. By MARCUS P. HATFIELD, A. M., M. D., Chicago. (*Chicago: G. P. Engelhard & Company, 1901.*)

This is a serviceable little volume of 135 pages in which the author treats of the following diseases of childhood: Scarlatina, measles, German measles, parotitis epidemica, pertussis, varicella, variola, and la grippe. It is a good epitome of our knowledge of these diseases brought up to date, and will be useful both to the student and practitioner.

Sajous's Annual and Analytical Cyclopædia of Practical Medicine. Volume VI, Diseases of Rectum and Anus to Zinc. (*Philadelphia, New York, Chicago: F. A. Davis Company Publishers, 1901.*)

This volume completes the first series of this work. The first one appeared in 1898, so that the subject-matter covered in the six volumes has been completed in about three years. The value of the entire work is much enhanced by the completion of this last volume, for we can now get information on practically all diseases and therapeutic remedies in the category from A to Z. This was not the case previous to the completion of the entire series, an objection which is always a serious one in any system in which the diseases are treated alphabetically.

The present volume contains articles on some important diseases which have been written by well-known authorities. Thus, the article on "Rheumatism," was written by Levison, of Copenhagen; "Diseases of the Stomach," by Stewart, of Philadelphia; "Surgery of the Stomach and Intestines," by Keen and Tinker, of Philadelphia; and "Yellow Fever," by Surgeon-General Wyman, of Washington.

The success of the Annual and Analytical Cyclopædia is in large part due to the editor and his admirable corps of associates. The general practitioner in particular will find the work a most useful reference hand-book.

Diseases of the Intestines. By DR. I. BOAS, Berlin. Authorized translation from the first German Edition with Special Additions. By SEYMOUR BASCH, M. D., New York City. (*New York: D. Appleton & Company, 1901.*)

This translation of Boas's admirable treatise on Diseases of the Intestines will be welcomed by physicians in this country. The author's reputation as an authority on stomach diseases is a sufficient guarantee that the subject has been carefully treated. It is the final volume of the author's work on diseases of the gastro-intestinal tract.

The volume contains 562 pages with 47 illustrations in the text. The first two introductory chapters deal with the anatomy, histology and physiology of the intestines. The subject-matter proper is divided into two parts. Part I deals with the methods of examination of the patient and of the intestinal contents. There is also a general consideration of the dietetic, hydrotherapeutic, electrical and medicinal treatment of intestinal diseases. Part II is devoted to the consideration of special intestinal diseases. We regret to observe that the author relies too much on the conservative treatment of appendicitis. This is unfortunate, as experience has shown that too many deaths from appendicitis are due to the general practitioner not recognizing the gravity of the disease and of the symptoms in individual cases. An author, in our opinion, cannot impress too strongly on physicians the great importance of having a surgeon see all cases of appendicitis early in the attack, so that much valuable time may be eventually gained should an operation be necessary. The translator, however, has done much to counteract the views of the author by insisting on the importance of early surgical interference in proper cases.

Diagnostics of Internal Medicine. By GLENTWORTH REEVE BUTLER, A. M., M. D., Brooklyn. (*New York: D. Appleton & Co., 1901.*)

When a new text-book on the Practice of Medicine or on Physical Diagnosis appears, one is led to make the mental comment, "Is it possible that there is place for still another?" We feel, however, that the author and publishers have been fully justified in placing this excellent work before the medical profession and particularly the students of medicine.

The volume comprises 1059 pages with five colored plates and 246 illustrations and charts in the text. The illustrations are unusually well executed and add much to the value of the work. The subject-matter is divided into two parts. The first part deals with the symptoms of disease and their indications, and occupies a total of 654 pages. This section, although not treating the subject of Physical Diagnosis in the usual way, includes everything that is usually taken up under this heading. An important feature of this part is the clear way in which the author has succeeded in explaining for the student and practitioner various phenomena of disease which often remain mysteries for years after one has commenced the study of medicine. The second part is devoted to the study of the various diseases and their characteristics as it is usually taken up in works on Practice of Medicine. The knowledge that has been acquired in the first part is brought into practical application in this section.

The volume is thoroughly up to date and little of value in the differential diagnosis of disease has escaped the author. We believe that the work will be found of great service to the students and practitioners.

Clinical and Pathological Papers from the Lakeside Hospital, Cleveland. Series 1, 1901.

This is the first volume of reports to appear from the Lakeside Hospital. It contains the more important papers that have been published from the hospital during the past year. There are eleven clinical and eight pathological and experimental papers. The volume is really a collection of reprints and consequently there is no uniformity in the quality of the paper nor in the letter-type used. Many of the papers are of great interest, but may not be reviewed as they have already been published in various American medical journals.

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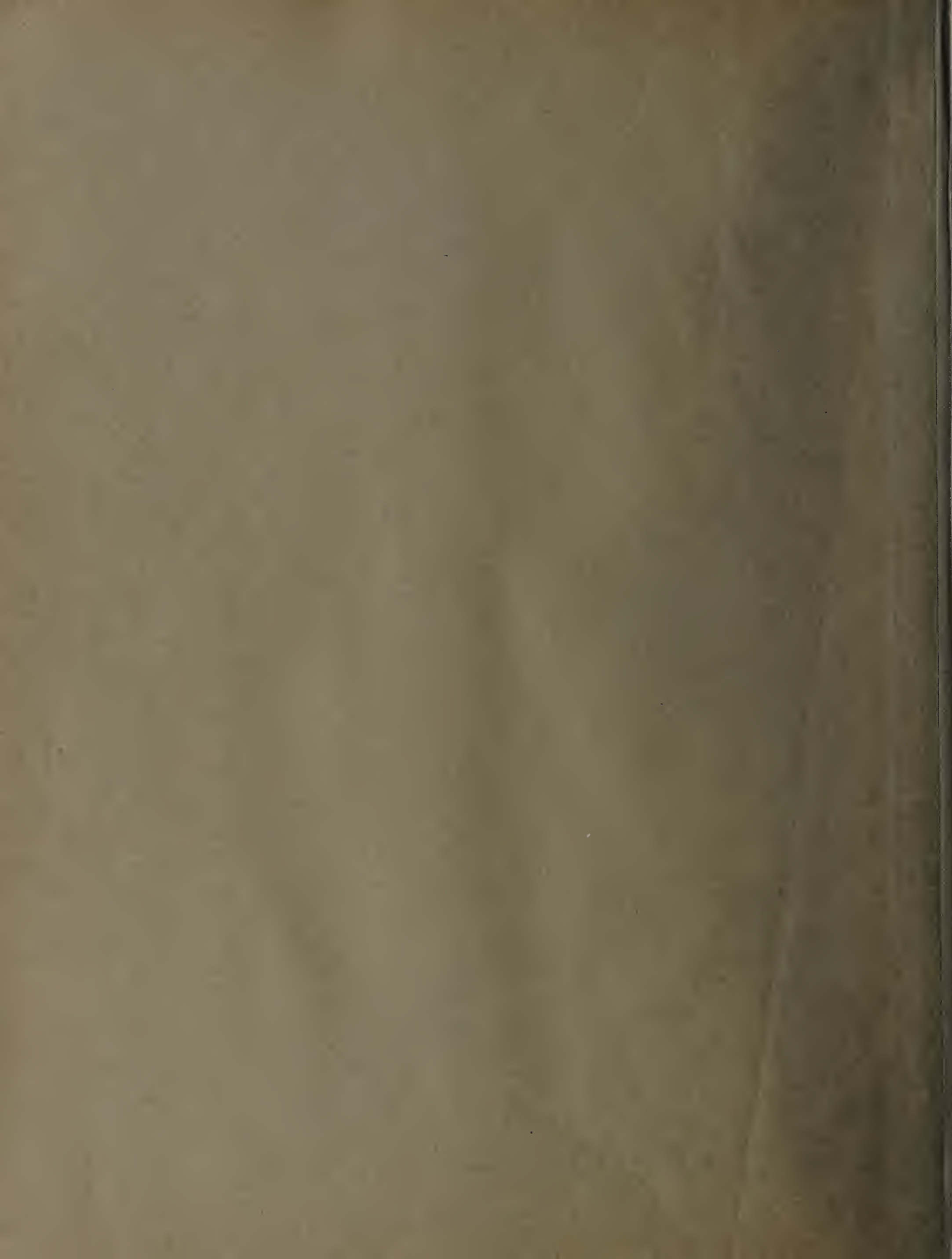
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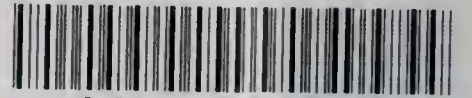
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